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Antipsychotic Medications

Model Curriculum

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American Society for Clinical Psychopharmacology

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Learning Objectives

- Residents will identify the major target symptoms of schizophrenia treatment
- Residents will become familiar with conventional and atypical antipsychotic medications
- Residents will recognize the major side effects of antipsychotic medications
- Residents will recognize the unique features of clozapine and depot antipsychotics

Outline

- Schizophrenia and Its Treatment
 - Clinical description and target symptoms
 - Dopamine hypothesis
- Antipsychotic medications
- Efficacy of antipsychotics
- Side effects of antipsychotics
 - Extrapyramidal symptoms
 - Cardiovascular
 - Mortality
 - Metabolic syndrome
 - Tardive dyskinesia
- Antipsychotic selection and treatment strategies

Pretest



-
1. Negative symptoms of schizophrenia include:
 - a. Auditory hallucinations
 - b. Blunted affect
 - c. Depressed mood
 - d. Persecutory delusions
 - e. Thought disorganization



Pretest

-
2. Clinical efficacy of antipsychotic medications is highly correlated with:
- a. Dopamine D1 binding
 - b. Dopamine D2 binding
 - c. Serotonin binding
 - d. The ratio of D1/D2 binding
 - e. The ratio of D2/serotonin binding
-

Pretest

-
3. Clozapine is unique among antipsychotics in that it:
- a. Has greater efficacy
 - b. Has fewer side effects
 - c. Is a dopamine D2 partial agonist
 - d. Is FDA approved for treatment of bipolar mania
 - e. Has a more favorable safety profile
-

Pretest

-
4. Which first-line atypical antipsychotic has the lowest risk of extrapyramidal side effects?
- a. Aripiprazole
 - b. Olanzapine
 - c. Quetiapine
 - d. Risperidone
 - e. Ziprasidone
-

Pretest

-
5. Which of the following atypical antipsychotics has the lowest risk of metabolic complications?
- a. Clozapine
 - b. Olanzapine
 - c. Quetiapine
 - d. Risperidone
 - e. Ziprasidone
-



Schizophrenia and Its Treatment



Definition



Schizophrenia is a chronic or recurrent disorder characterized by

- Periods of psychosis
- Long-term functional deterioration



Symptom Subtypes in Schizophrenia

Positive Symptoms

- Delusions
- Hallucinations
- Thought Disorganization
- Catatonia


Cognitive Deficits

- Memory
- Attention
- Language
- Executive Function

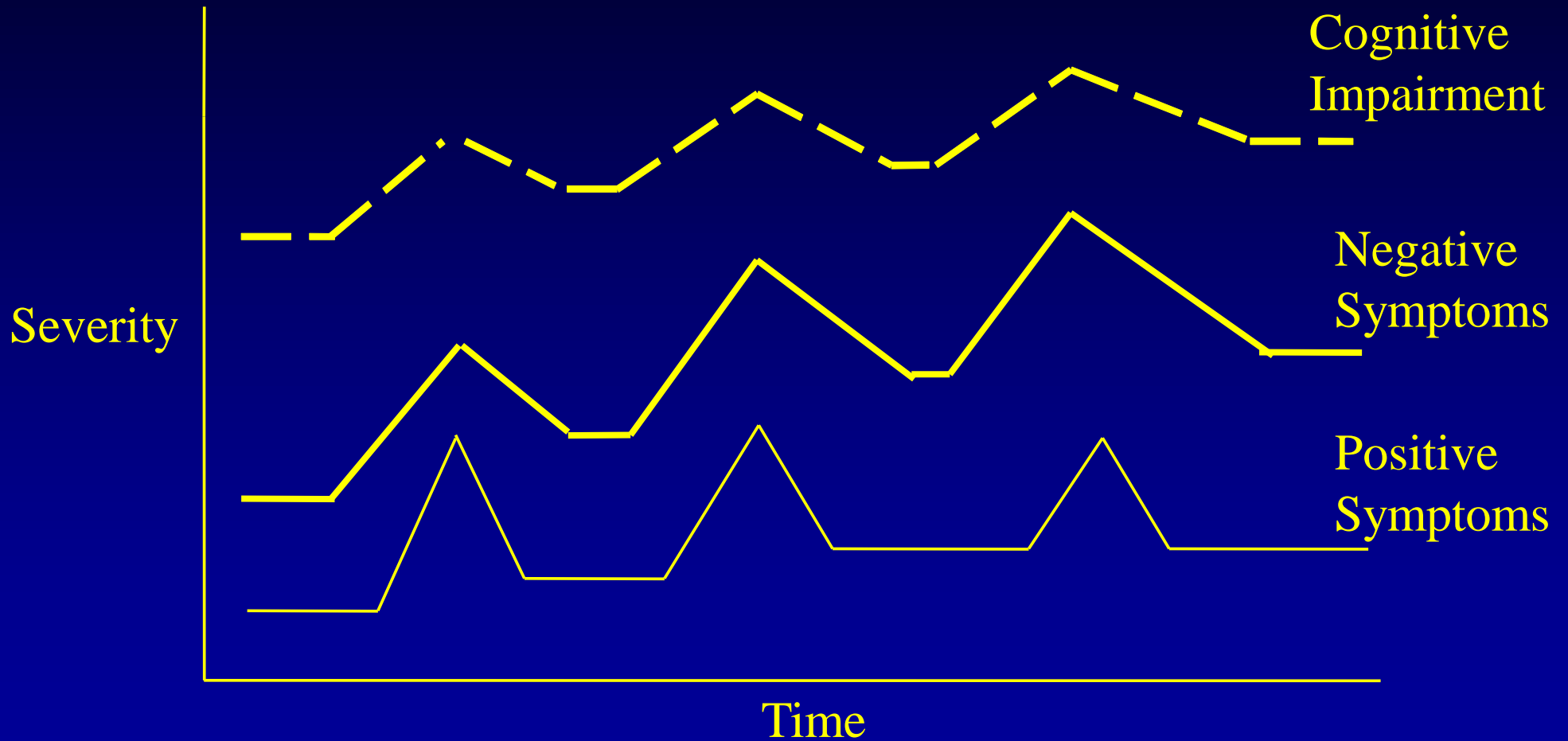
Negative Symptoms

- Blunted Affect
- Anhedonia/Asociality
- Alogia
- Inattention
- Avolition/Apathy

Mood Symptoms

- Depression
 - Dysphoria
 - Suicidality
-
- 

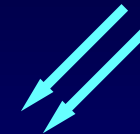
Course of Symptom Subtypes



Contributions to Functional Impairment

Positive Symptoms

Negative Symptoms



Social/Occupational Dysfunction

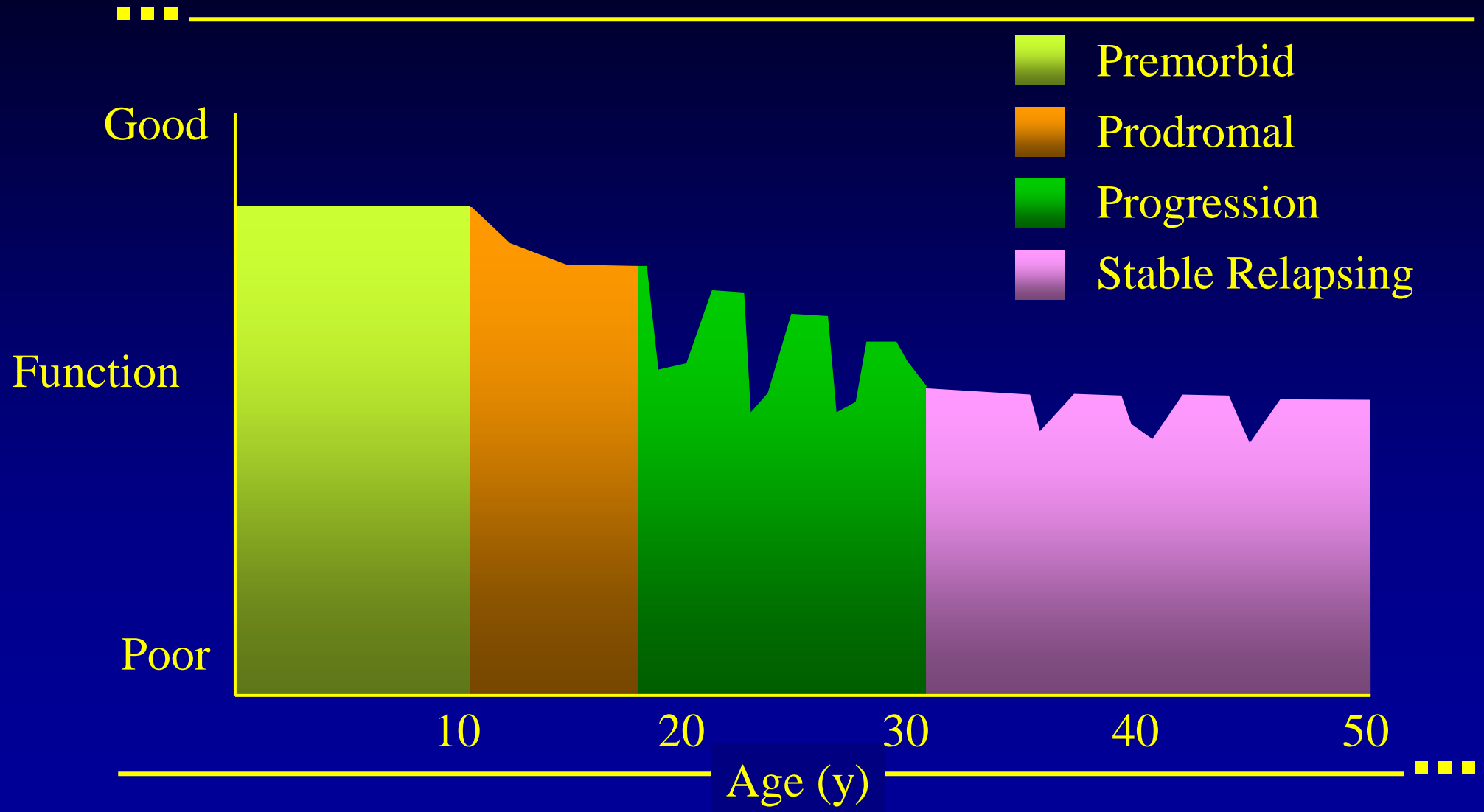
- work
- interpersonal relationships
- self care



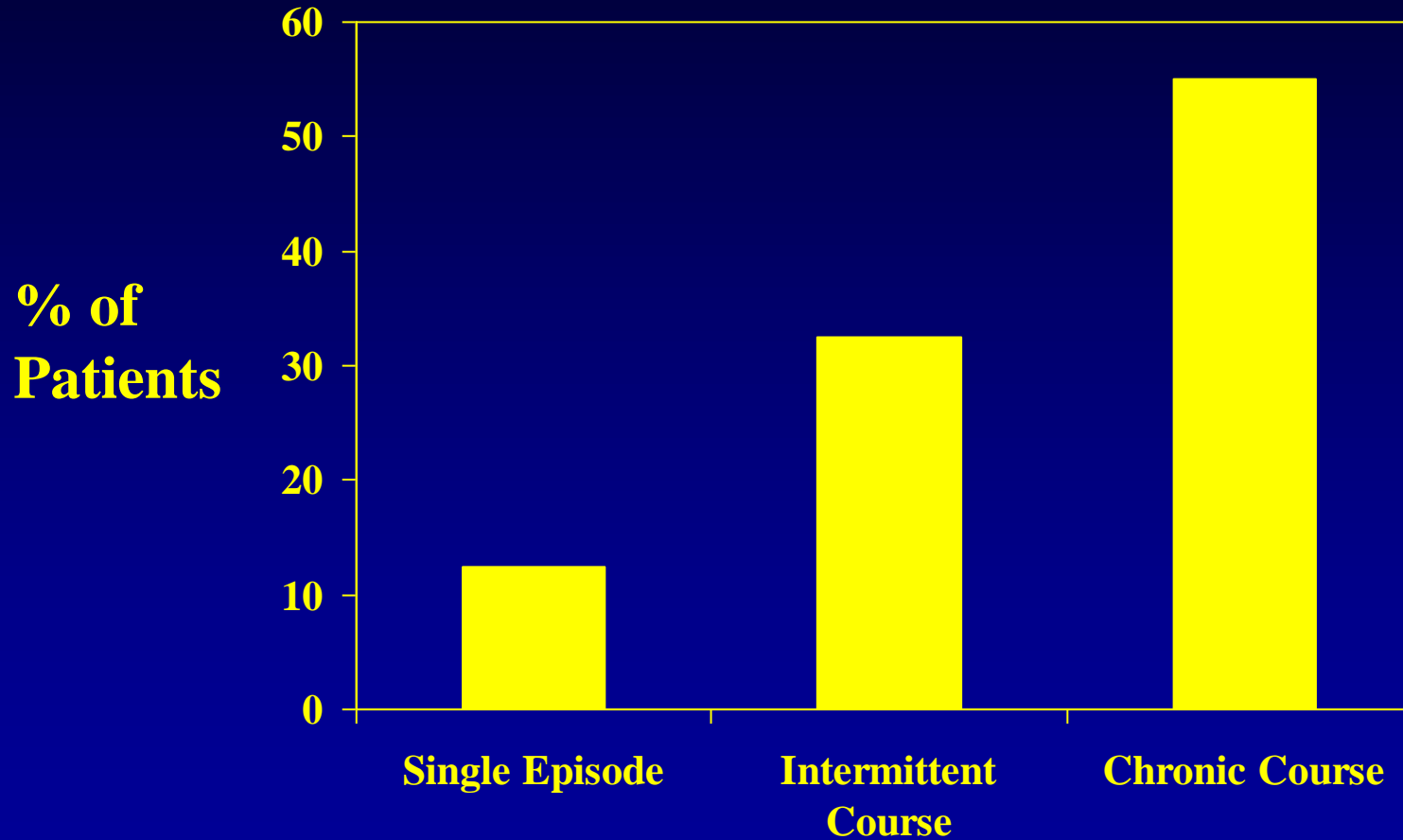
Cognitive Symptoms

Mood Symptoms

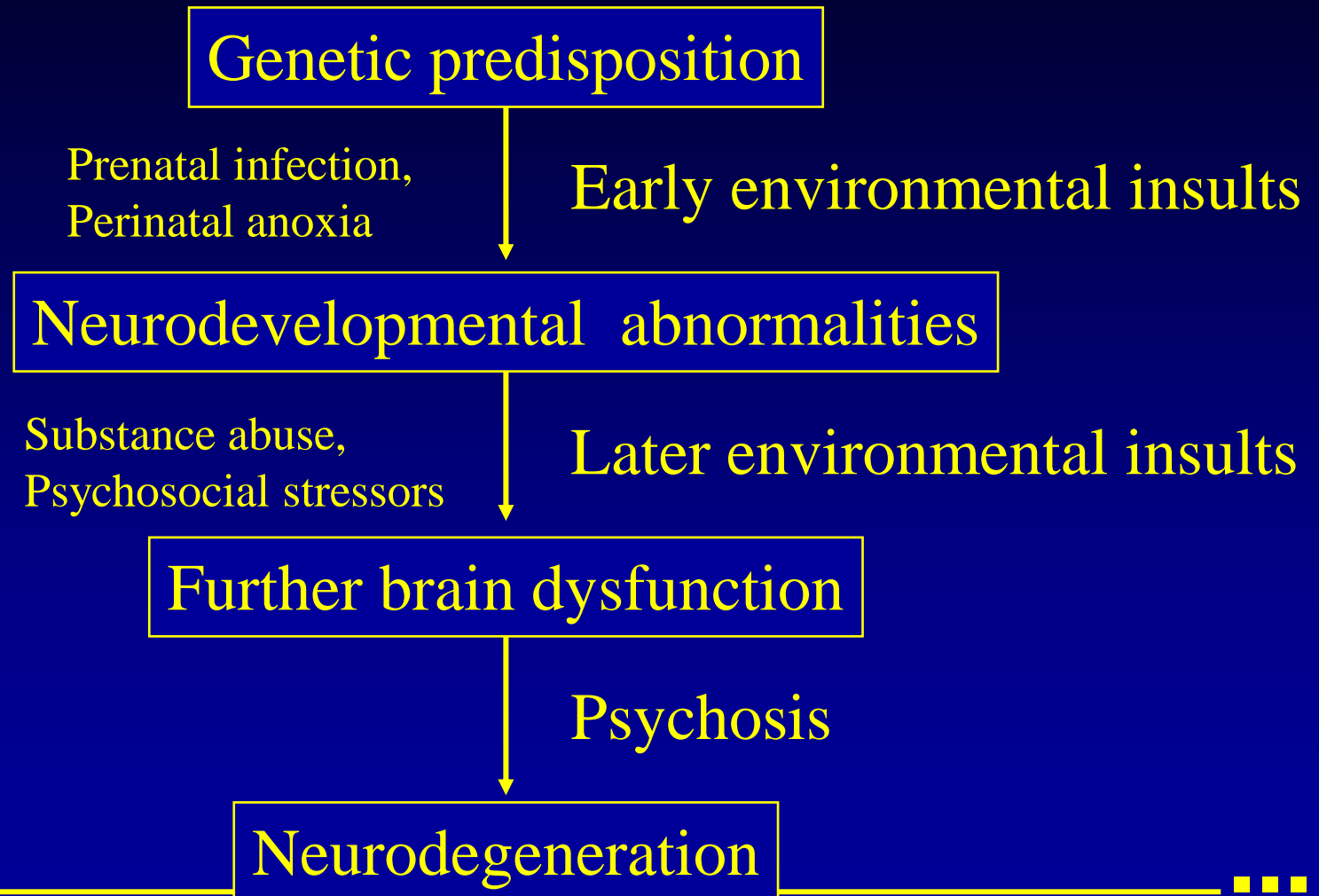
Natural History of Schizophrenia



Natural History of Schizophrenia



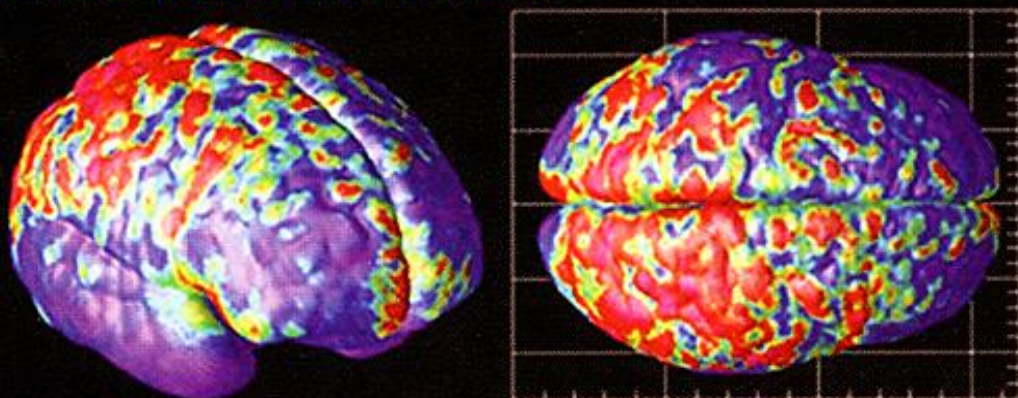
Etiology of Schizophrenia



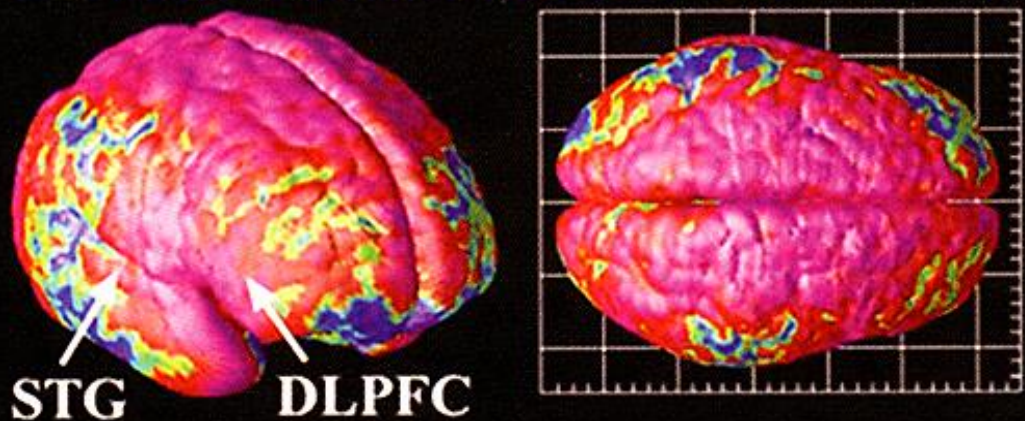
Structural Abnormalities in Schizophrenia

Early and Late Gray Matter Deficits in Schizophrenia

EARLIEST DEFICIT



5 YEARS LATER (SAME SUBJECTS)




STG

DLPFC


Average
Deficit



Thompson
et al., 2001

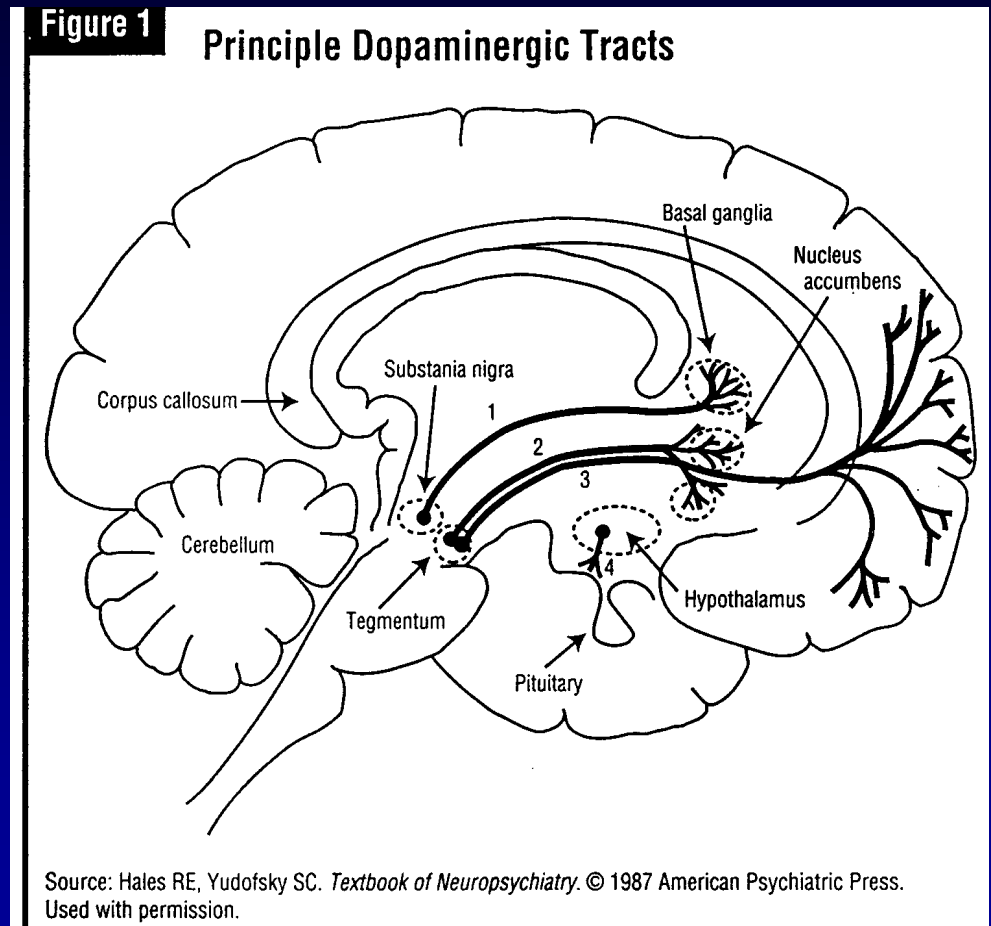


Dopamine Hypothesis of Schizophrenia



Major Dopamine Pathways

1. Nigrostriatal tract- (extrapyramidal pathway) begins in the substantia nigra and ends in the caudate nucleus and putamen of the basal ganglia
2. Mesolimbic tract - originates in the midbrain tegmentum and innervates the nucleus accumbens and adjacent limbic structures
3. Mesocortical tract - originates in the midbrain tegmentum and innervates anterior cortical areas
4. Tuberoinfundibular tract - projects from the arcuate and periventricular nuclei of the hypothalamus to the pituitary



Dopamine Hypothesis

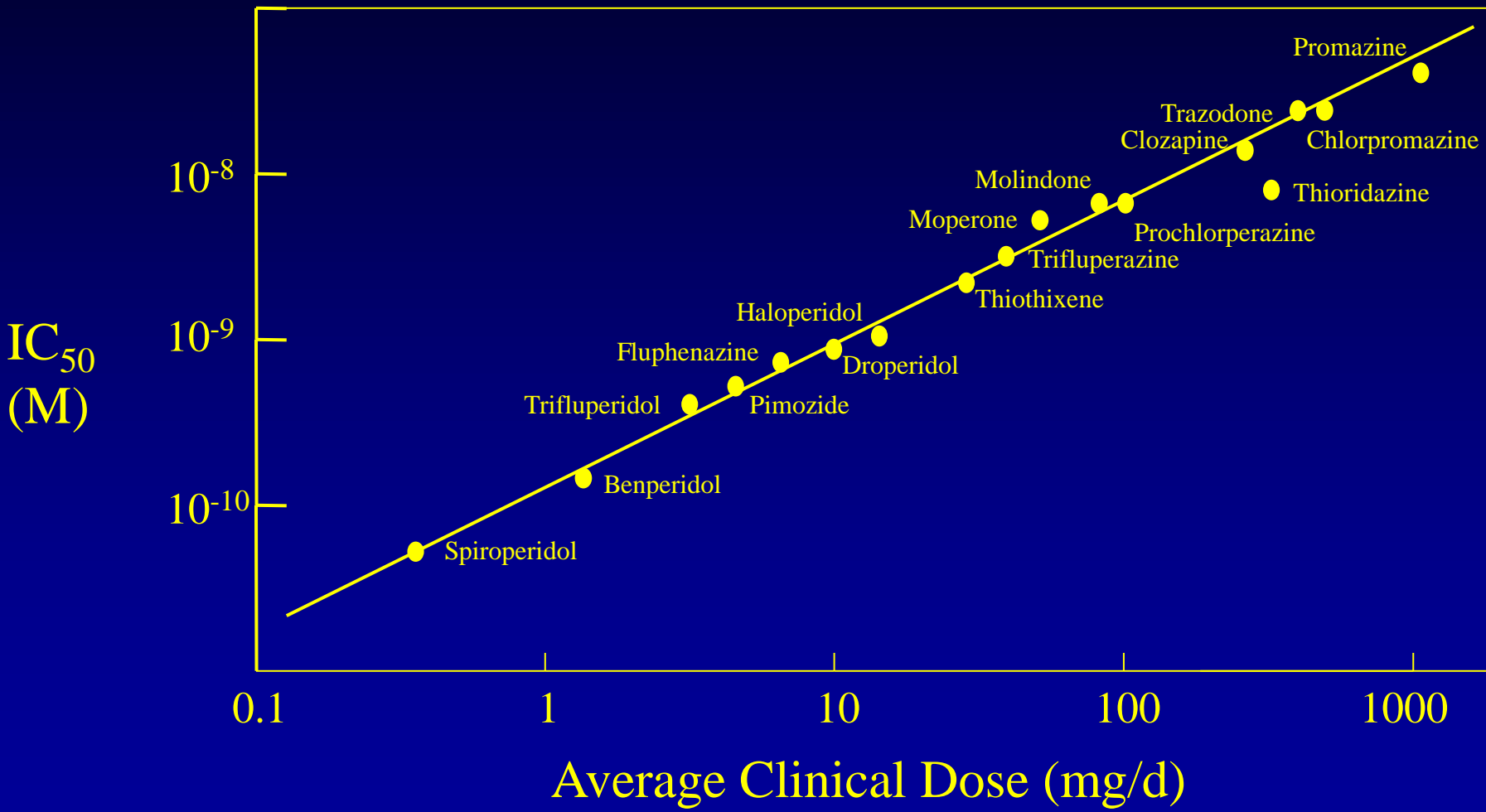


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- Clinical efficacy of antipsychotics correlates with dopamine D₂ blockade
 - Psychotic symptoms can be induced by dopamine agonists



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Clinical Efficacy and Dopamine D₂ Blockade



Dopamine Hypothesis



- Normal subjects have 10% of dopamine receptors occupied at baseline
- Schizophrenic subjects have 20% of dopamine receptors occupied at baseline



Dopamine Receptor Subtypes

D₁ Family

- D₁ and D₅ receptors
- Poor correlation with antipsychotic activity
- D₁ family may modulate effects of D₂ family

D₂ Family

- D₂, D₃, D₄ receptors
- High correlation with antipsychotic activity
- D₄ is prominent in limbic structures, but absent from extrapyramidal pathways
- Atypical antipsychotics have high D₄ affinity



Dopamine D₂ Effects

Possible Benefit

- Antipsychotic effect

Possible Side Effects

- EPS
 - dystonia
 - parkinsonism
 - akathisia
 - tardive dyskinesia
- Endocrine changes:
 - prolactin elevation
 - galactorrhea
 - gynecomastia
 - menstrual changes
 - sexual dysfunction

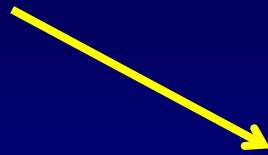


Dopamine and Antipsychotics

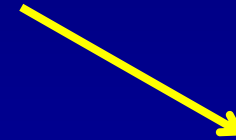
- 65% D₂ receptor occupancy is required for efficacy
- 80% D₂ receptor occupancy is correlated with EPS
- Shorter time of D₂ receptor occupancy is correlated with lower EPS

Dopamine Hypothesis

Subcortical
Dopamine
Excess



D₂
Hyperstimulation



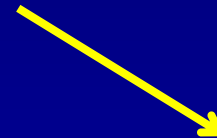
Positive
Symptoms

Dopamine Hypothesis

■ ■ ■
Prefrontal
Dopamine
Deficit



D₁ & D₂
Hypostimulation



Cognitive
& Negative
Symptoms
■ ■ ■

Negative Symptoms

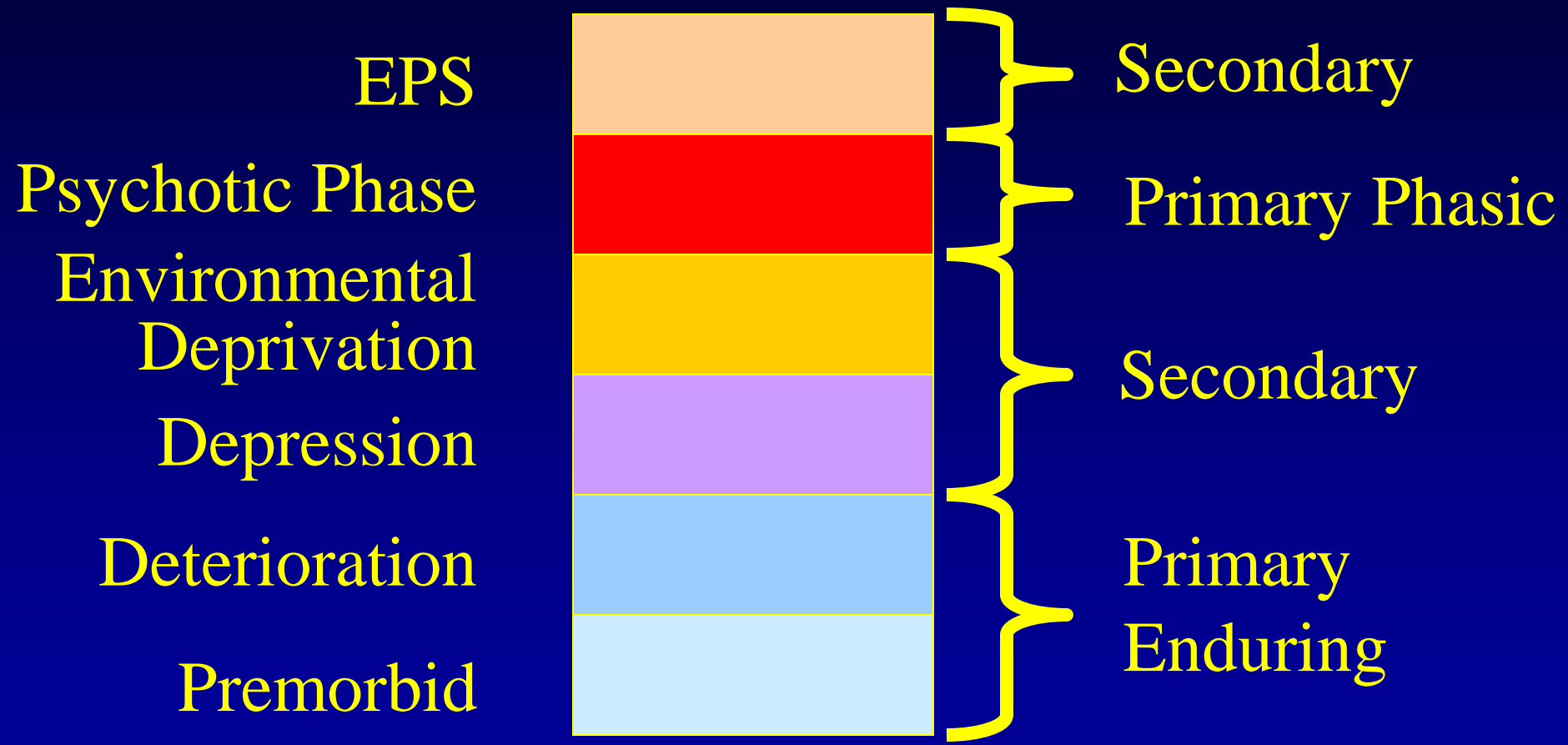


How do antipsychotics improve negative symptoms?

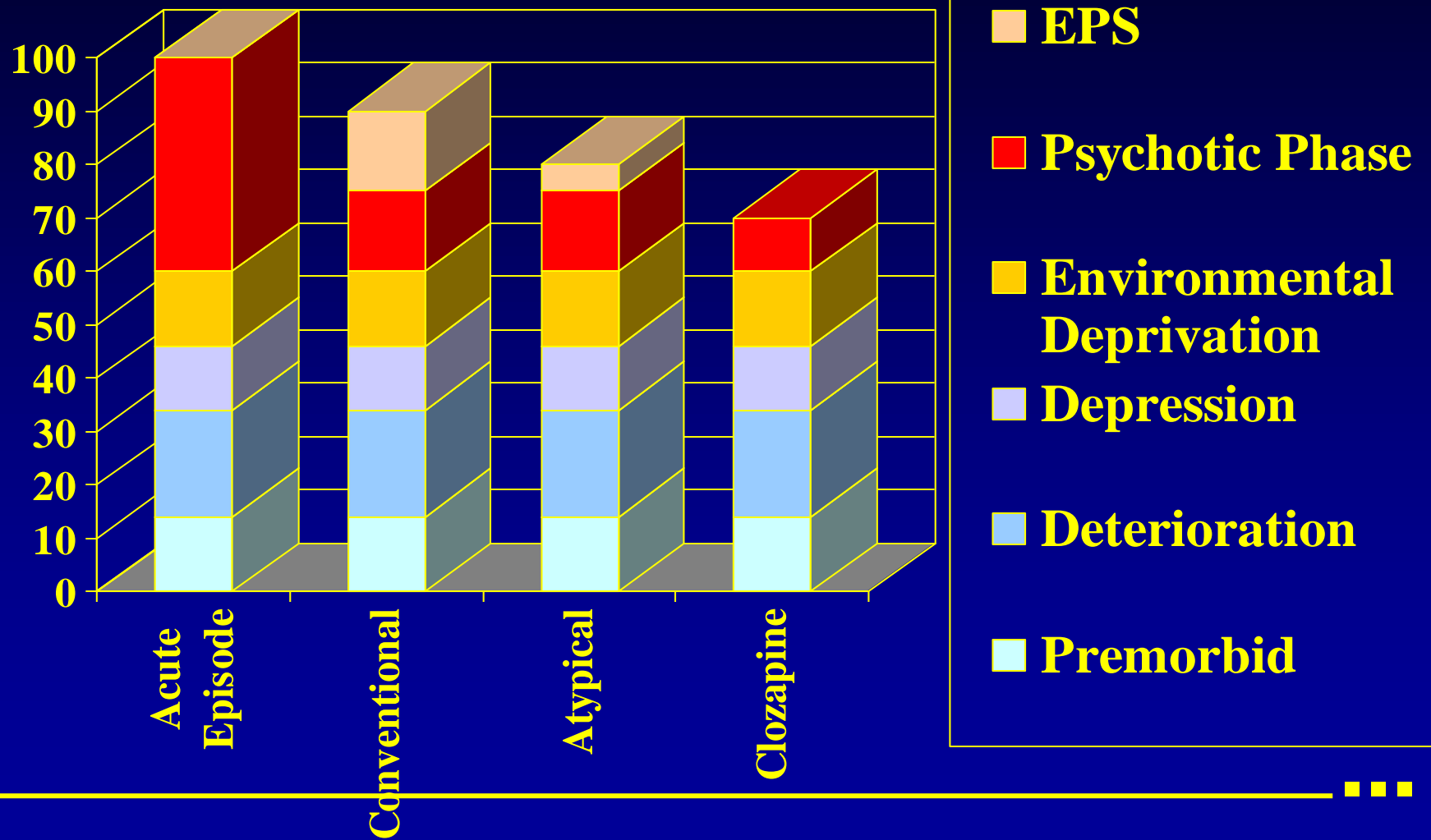


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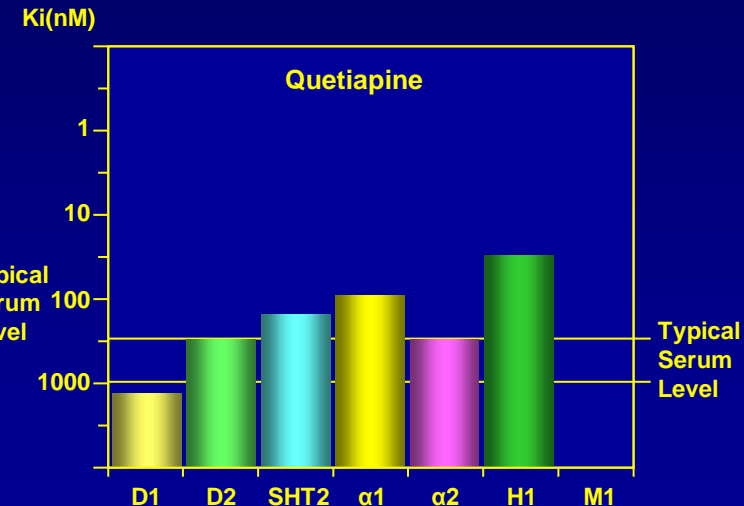
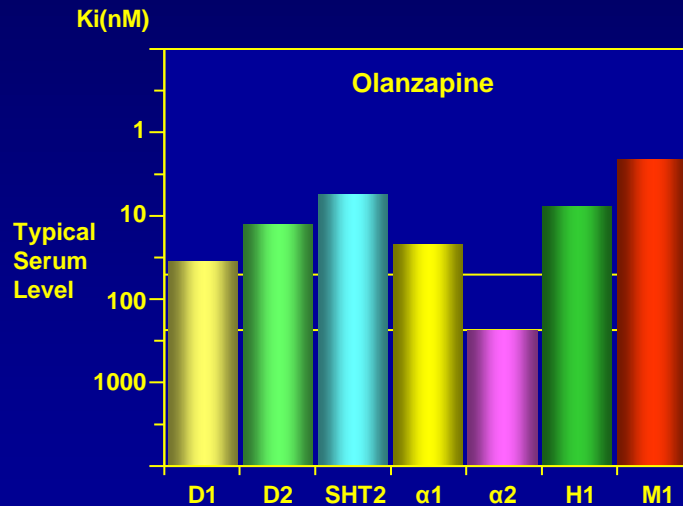
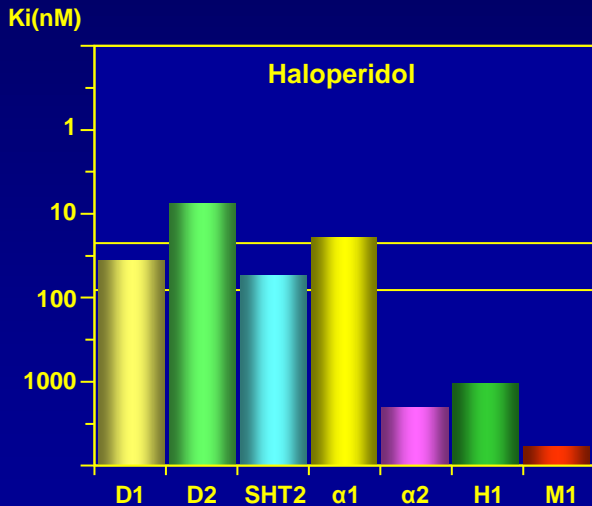
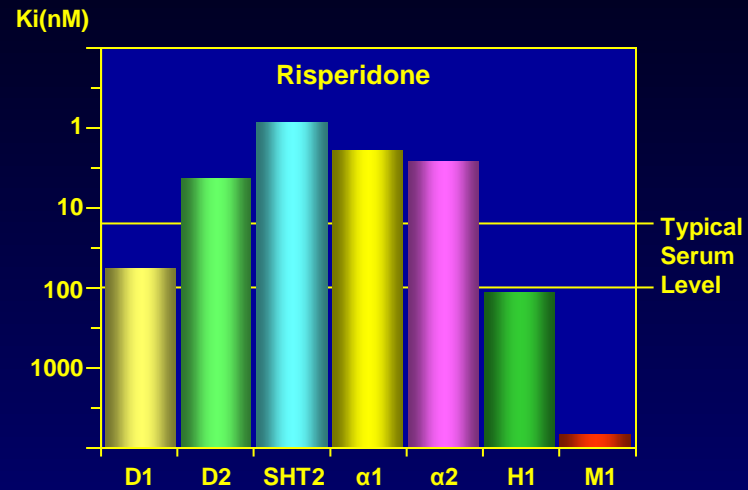
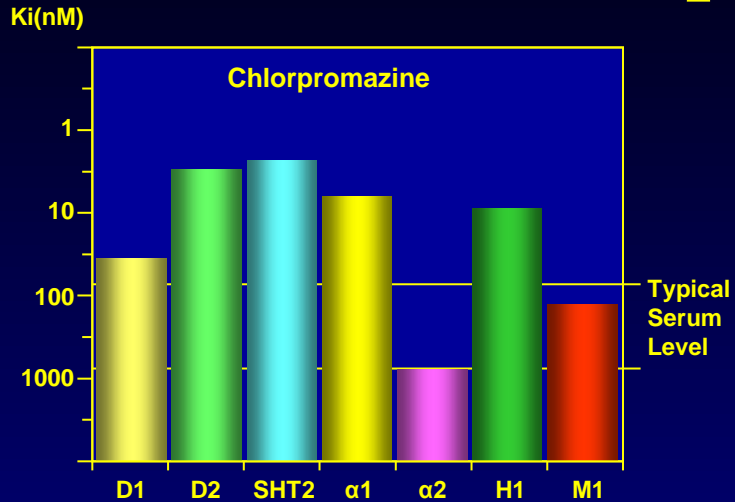
Negative Symptom Components



Negative Symptom Components



Receptor Profiles



Adapted from Jibson MD & Tandon R, J Psychiatric Res 1998;32, 215. Data from Beasley et al. (1996a, 1996b), Saller and Salama (1993), Seeger et al. (1995), Baldessarini and Frankenburg (1991), Thyrum et al. (1996), Dahl (1986), Heykants et al. (1994).

Serotonin

- Atypical antipsychotics are high in serotonin activity
 - Serotonin agonists (e.g., LSD) produce psychotic symptoms
 - Dopaminergic activity is modulated by serotonin
but
 - Studies of serotonin in the brains of schizophrenic patients have been equivocal
-



Pharmacologic Treatment of Schizophrenia



Target Symptoms



-
- Active psychosis
 - most common reason for hospitalization
 - most responsive to medications
 - Negative symptoms
 - poor response to medication
 - progress most rapidly during early acute phases of illness



Target Symptoms

- ■ ■

 - Cognitive impairment
 - may be improved or worsened by medications
 - Functional deterioration
 - Highly correlated with cognitive symptoms
 - Moderately correlated with negative symptoms
 - Occurs mostly during acute episodes, which can be prevented by medications
-



Antipsychotic Medications



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FDA Approved Indications for Antipsychotic Medications

■ ■ ■ Adults

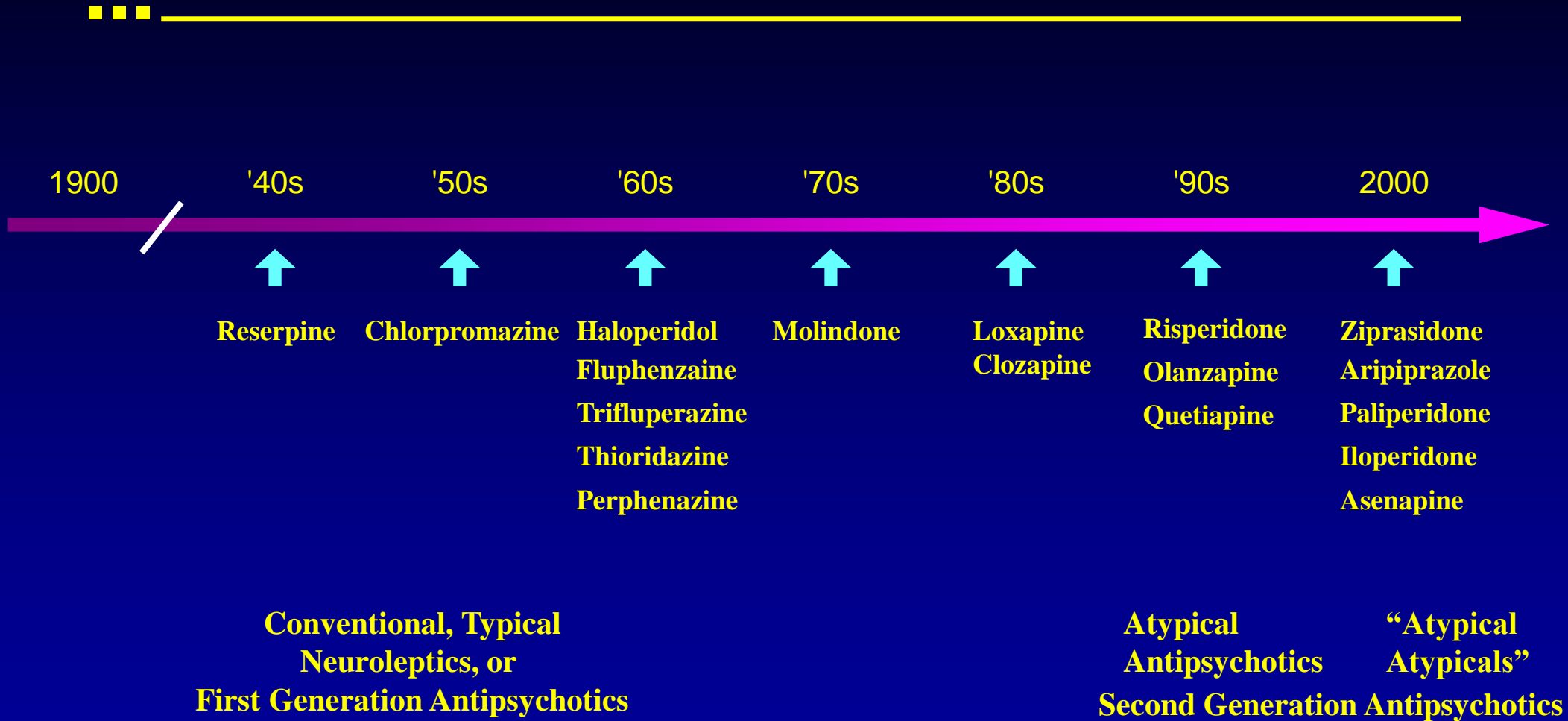
- Schizophrenia (acute and maintenance)
- Bipolar disorder (acute mania, maintenance, bipolar depression)
- Agitation associated with schizophrenia or bipolar disorder

Children and Adolescents

- Schizophrenia
 - Autism
-



The Evolution of Antipsychotic Medications



* Conventional Antipsychotic Medications (Neuroleptics)

- Chlorpromazine (Thorazine) introduced in 1952
 - Several classes (phenothiazines, butyrophenones, thioxanthenes, indoles, benzamides, etc) introduced in the 1950s and 1960s
 - Principal pharmacological activity is D₂ blockade
 - Variable activity at H₁, M₁, and α₁ receptors
 - High risk of EPS and tardive dyskinesia
-

* Conventional Antipsychotic Medications (Neuroleptics)

High Potency

- High EPS risk
 - Weaker anticholinergic effects
 - Most common agents
 - Haloperidol (Haldol)
 - Fluphenazine (Prolixin)
 - Perphazine (Trilafon)
 - Thiothixine (Navane)
-

* Conventional Antipsychotic Medications

High Potency

- Advantages

- Injectable formulations (including IV)
- Depot formulations
- Inexpensive

- Disadvantages

- High risk of EPS
 - High risk of tardive dyskinesia
-

* Conventional Antipsychotic Medications (Neuroleptics)

Low Potency

- Lower EPS risk
- Stronger anticholinergic effects
- Most common agents
 - Chlorpromazine (Thorazine)
 - Thioridazine (Mellaril)
 - Mesoridazine (Serentil)



* Conventional Antipsychotic Medications

Low Potency

- Advantages
 - Highly sedating
 - Injectable formulations
 - Inexpensive
 - Disadvantages
 - High risk of QTc prolongation
 - High risk of tardive dyskinesia
-

*

Atypical Antipsychotics (Second Generation Antipsychotics)

- Developed on the basis of receptor activity in addition to D₂ blockade
 - Fewer EPS
 - Decreased incidence of tardive dyskinesia
-

Atypical Antipsychotics



-
- Broader spectrum of activity
 - Some benefit for negative and cognitive symptoms
 - Beneficial for treatment-refractory patients (clozapine only)



Atypical Antipsychotics

- Aripiprazole (Abilify)
 - Asenapine (Saphris)
 - Iloperidone (Fanapt)
 - Olanzapine (Zyprexa)
 - Paliperidone (Invega)
 - Quetiapine (Seroquel)
 - Risperidone (Risperdal)
 - Ziprasidone (Geodon)
 - Clozapine (Clozaril) – Second-line use only
-

Aripiprazole



-
- Advantages
 - Unique pharmacology (partial agonist)
 - Disintegrating tablet and injectable formulations
 - Long clearance half-time
 - Disadvantages
 - Unpredictable response when combined with dopamine antagonists
 - Moderate-high cost



Asenapine



-
- Advantages
 - Sublingual administration
 - Newly approved
 - Disadvantages
 - Limited clinical experience
 - Twice-daily dosing
 - Moderate-high cost



Iloperidone



-
- Advantages
 - Newly approved
 - Disadvantages
 - Limited clinical experience
 - Twice-daily dosing
 - Moderate-high cost



Olanzapine



-
- Advantages
 - Extensive clinical experience
 - Long clearance half-time
 - Disintegrating tablet and injectable forms
 - Disadvantages
 - High risk of weight gain and metabolic syndrome
 - Moderate-high cost



Paliperidone



-
- Advantages
 - Does not require hepatic metabolism
 - Depot formulation
 - Disadvantages
 - Dose-dependent EPS
 - Moderate risk of weight gain
 - Prolactin elevation
 - Moderate-high cost



Quetiapine



-
- Advantages
 - Lowest EPS risk
 - Rapid onset of action
 - Sedating
 - Disadvantages
 - Longer dose titration
 - Moderate risk of weight gain
 - Moderate-high cost



Risperidone



-
- Advantages
 - Extensive clinical experience
 - Liquid, disintegrating tablet, and depot preparations
 - Generic available
 - Disadvantages
 - Dose-dependent EPS
 - Moderate risk of weight gain
 - Prolactin elevation



Ziprasidone



-
- Advantages
 - Low risk of weight gain
 - Low risk of sexual dysfunction
 - Injectable formulation
 - Disadvantages
 - Twice-daily dosing
 - Dosing with meals recommended
 - qTc prolongation



Clozapine

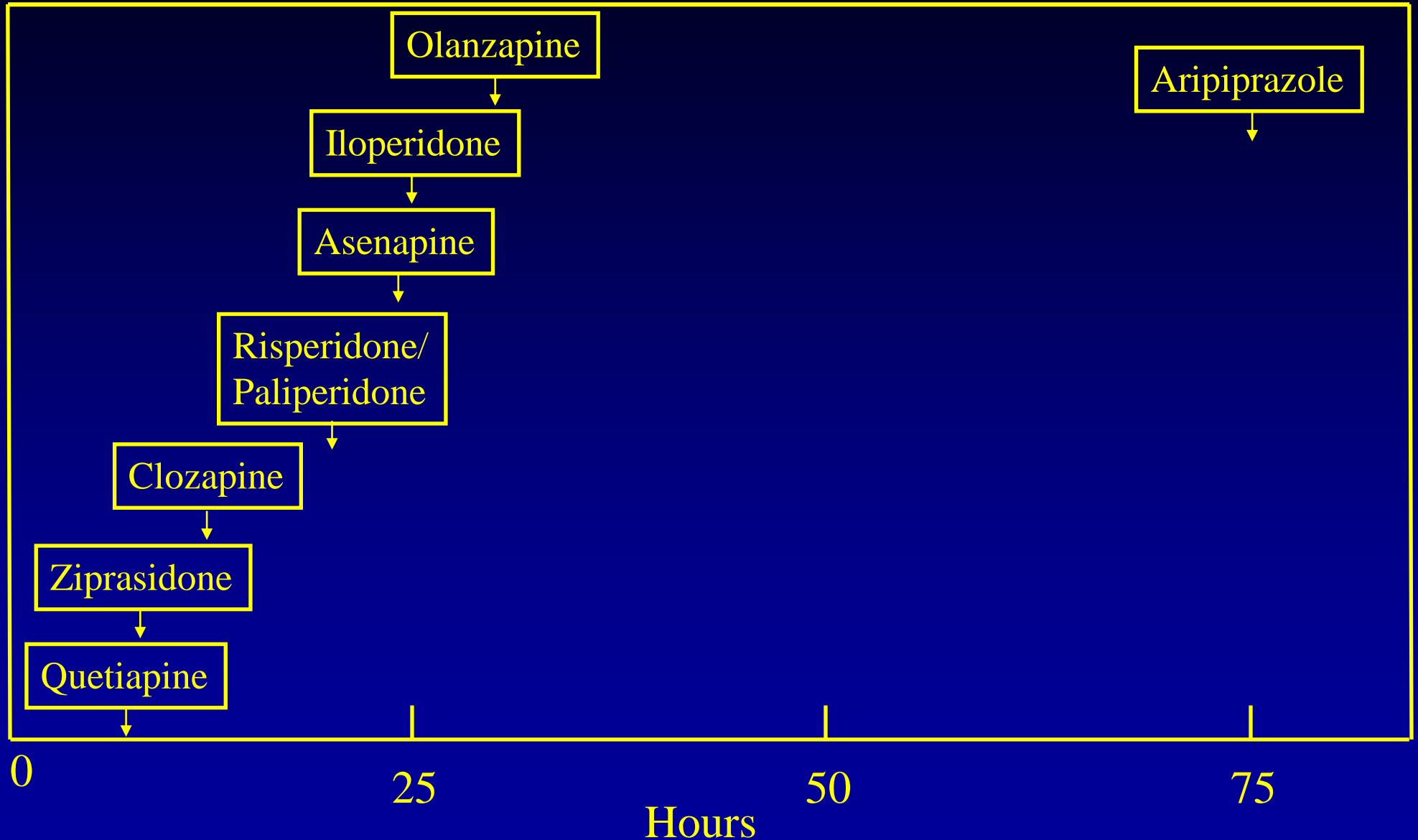
- Advantages

- Effective for 30-50% of treatment-refractory patients
- Most effective for negative symptoms
- Only proven treatment for TD

- Disadvantages

- Risk of agranulocytosis
 - Weekly, biweekly, or monthly blood draws
 - Unfavorable side effect profile
-

Elimination Half-Times



Depot Antipsychotics



-
- Fluphenazine (Prolixin) decanoate
 - Haloperidol (Haldol) decanoate
 - Paliperidone palmitate (Invega Sustenna)
 - Risperidone depot (Risperdal Consta)





Depot Antipsychotics



Medication	Dosing Frequency
Fluphenazine decanoate	1-2 wks
Haloperidol decanoate	2-4 wks
Paliperidone palmitate	4 wks
Risperidone depot	2 wks



Depot Antipsychotics



-
- Advantages
 - Ensured compliance
 - Lower total doses compared with oral medication may reduce side effects
 - Disadvantages
 - Poor patient acceptance
 - Minimal flexibility in dosing
 - Higher cost



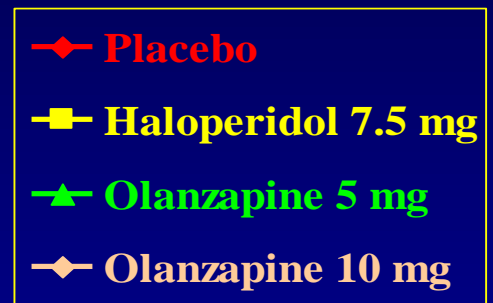
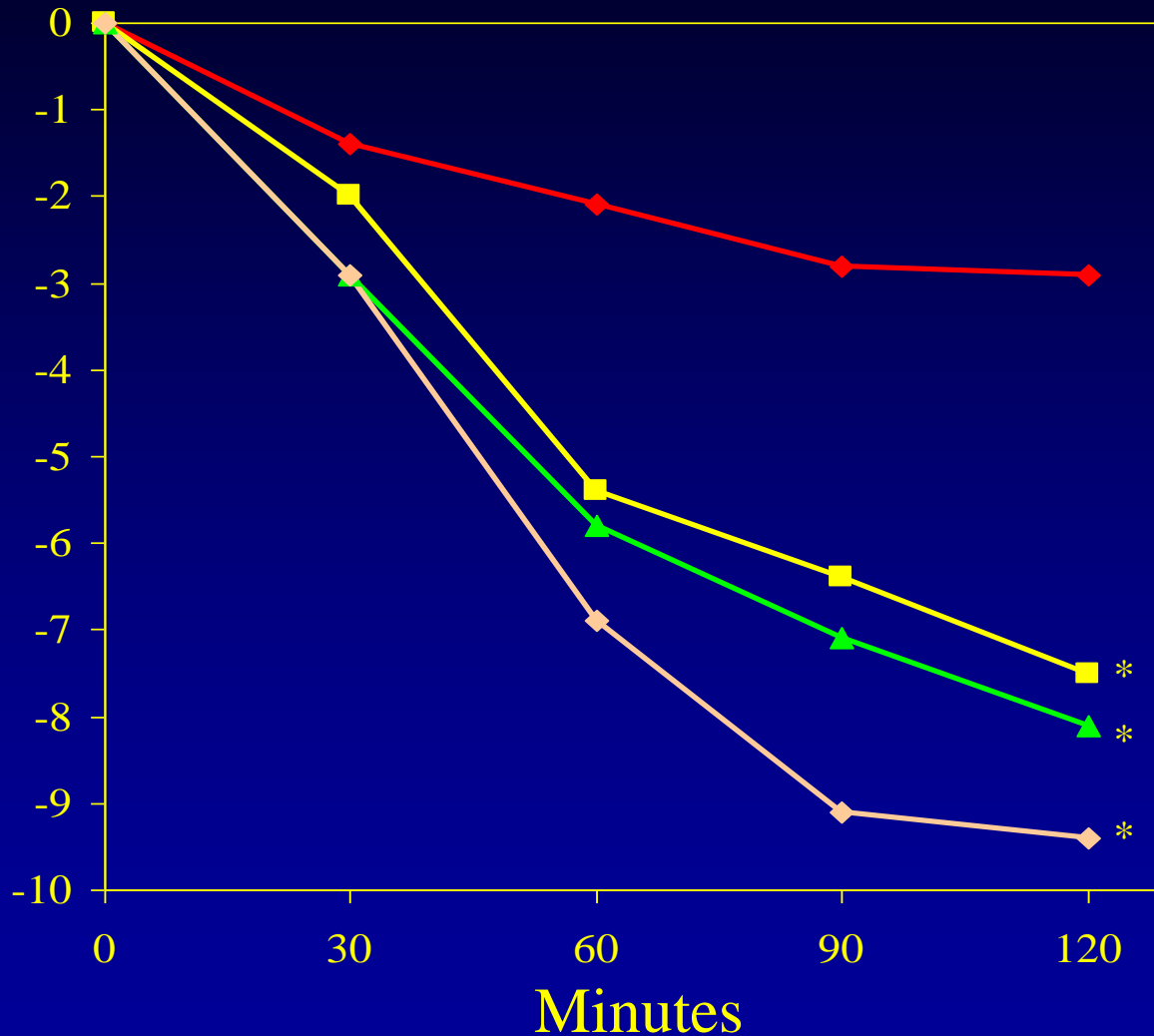


Efficacy of Antipsychotics



Injectable Olanzapine for Acute Agitation

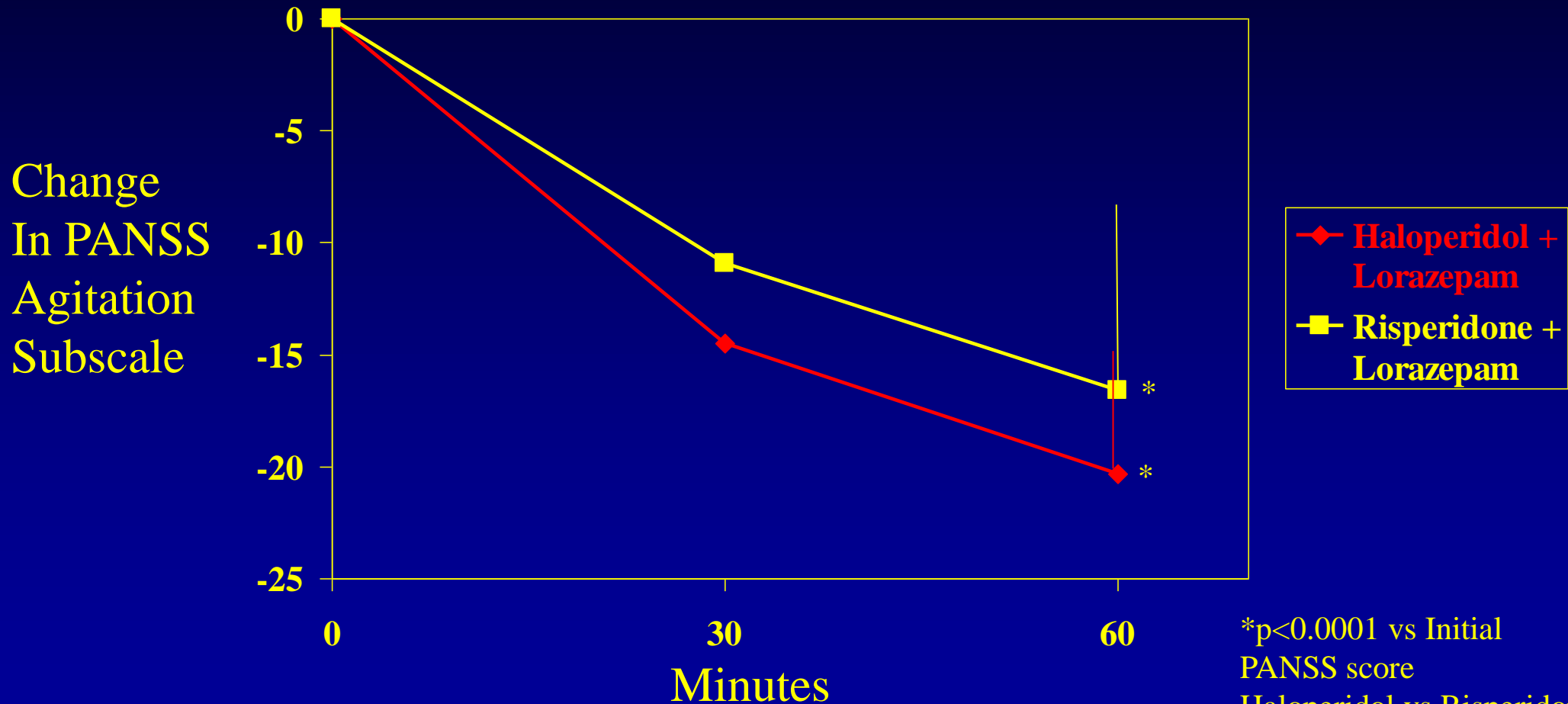
Change
In PANSS
Agitation
Subscale



* $p < 0.001$ vs Placebo

Olanzapine vs Haloperidol
not significant

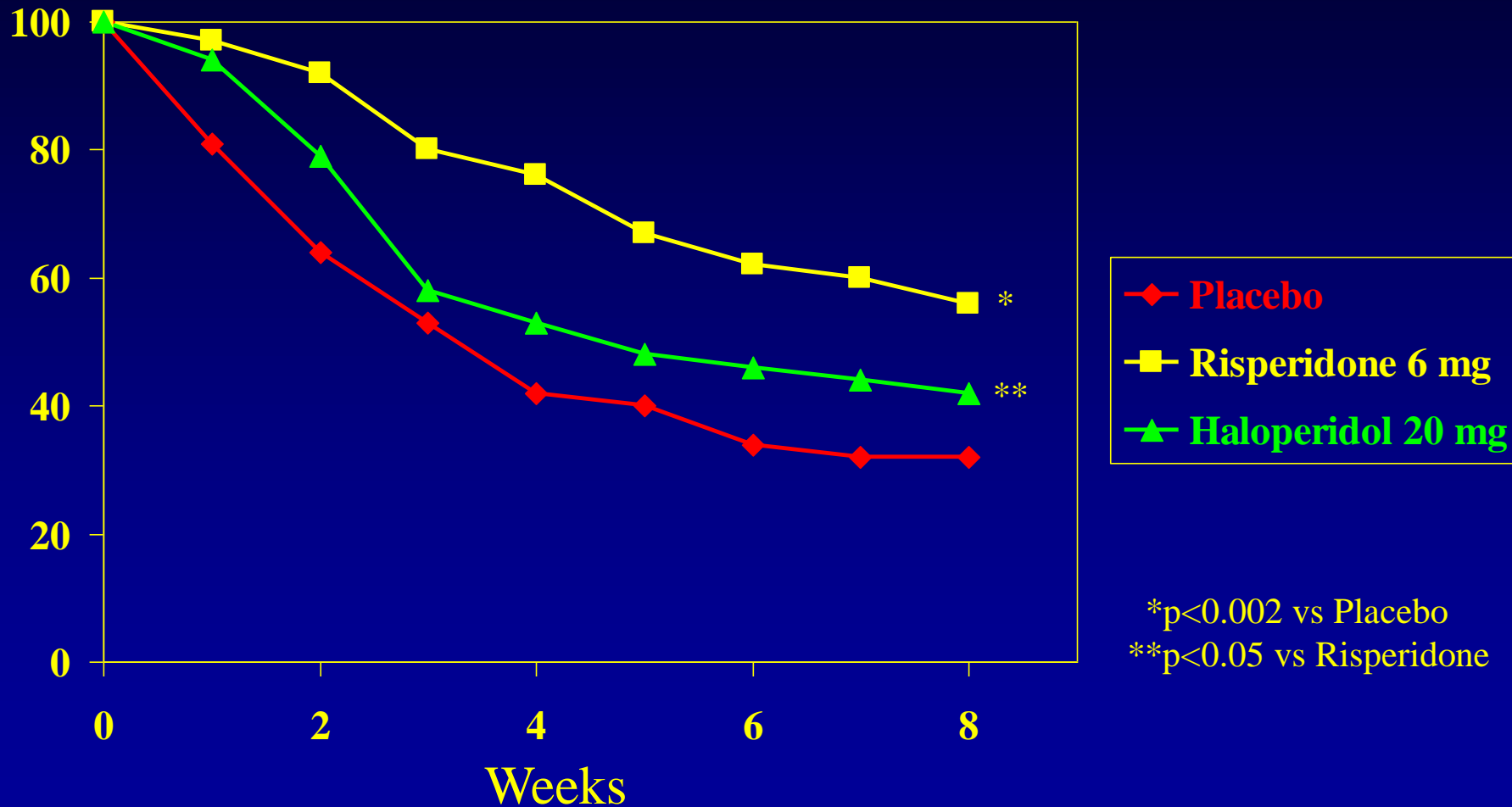
Oral Risperidone vs IM Haloperidol for Acute Agitation



*p<0.0001 vs Initial PANSS score
Haloperidol vs Risperidone not significant

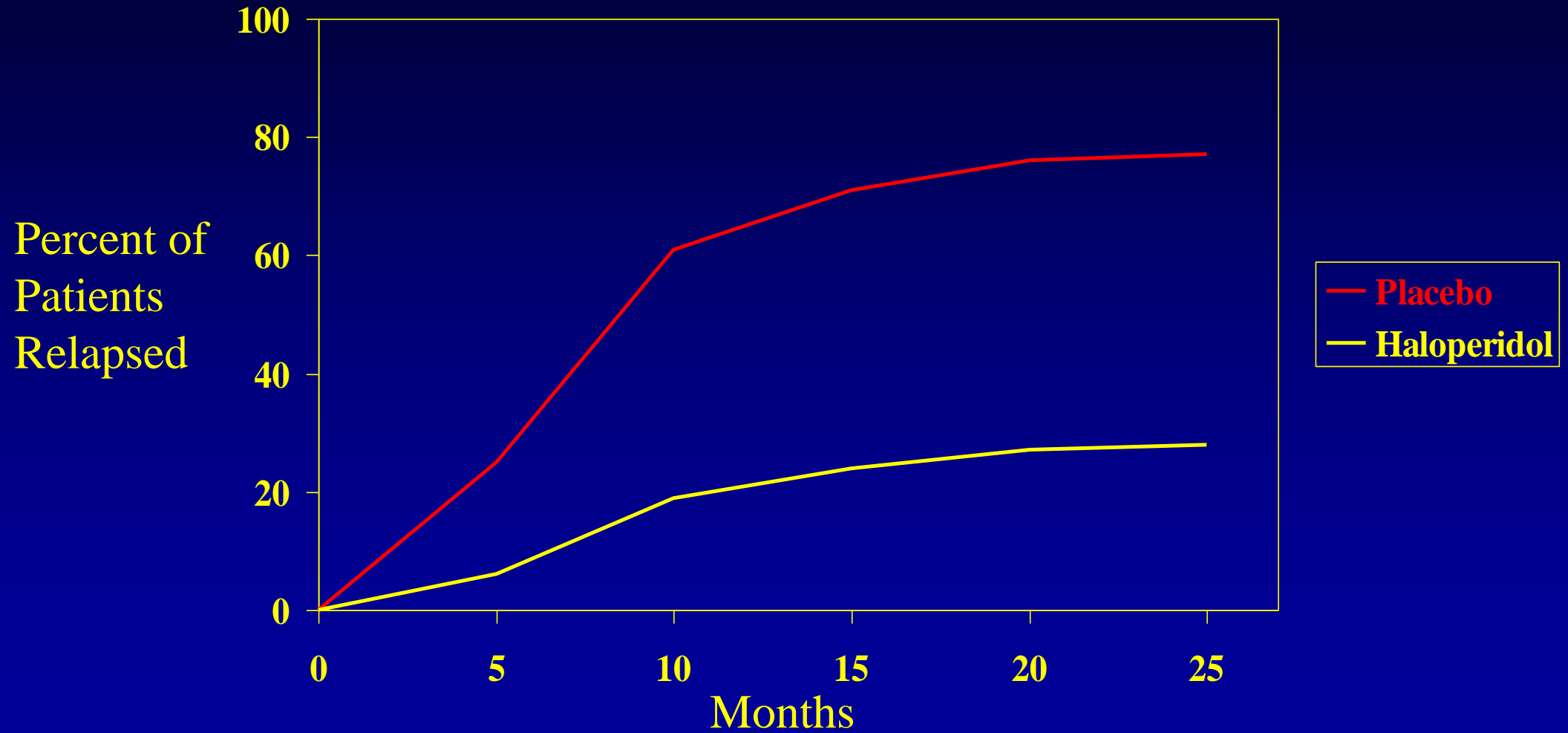
Risperidone for Short-term Treatment

Percent of Patients Remaining In Study



*

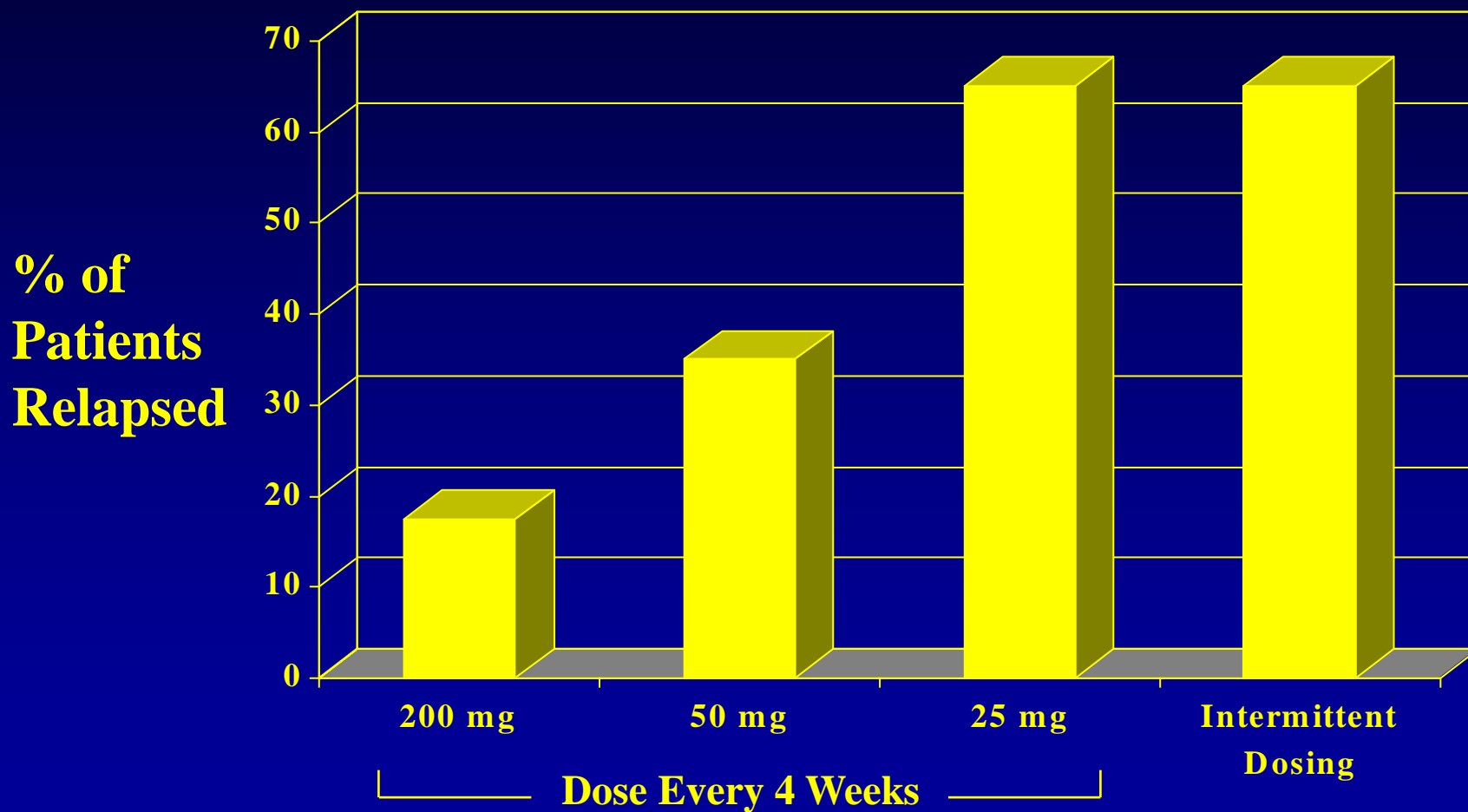
Haloperidol for Long-term Prevention of Relapse



*

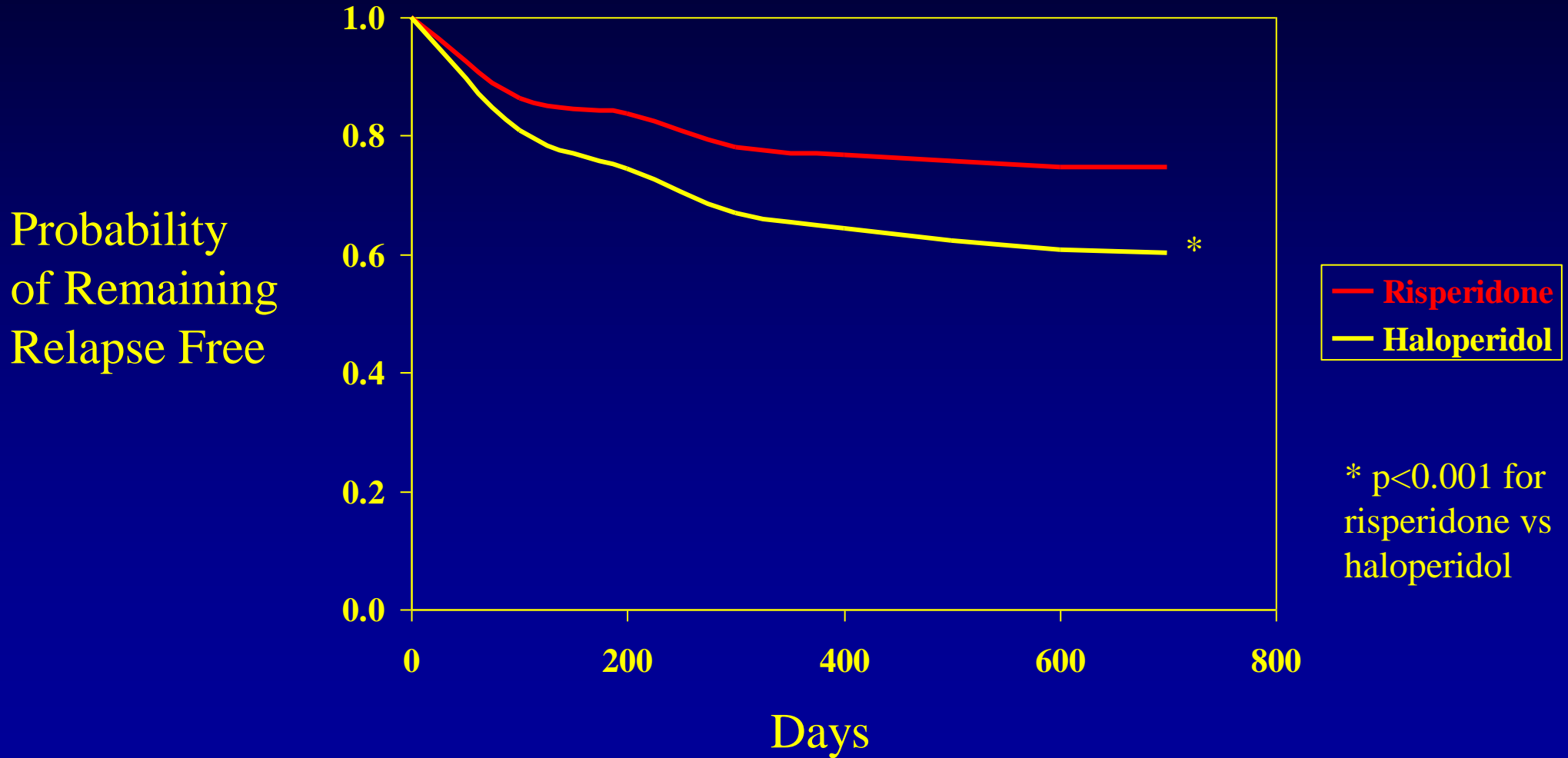
Relationship between Medication Dose and Relapse

1 Year of Haloperidol Decanoate Treatment



*

Risperidone for Long-term Prevention of Relapse



Mean Change in PANSS Score at 2 Years

P-Value

.001

.004

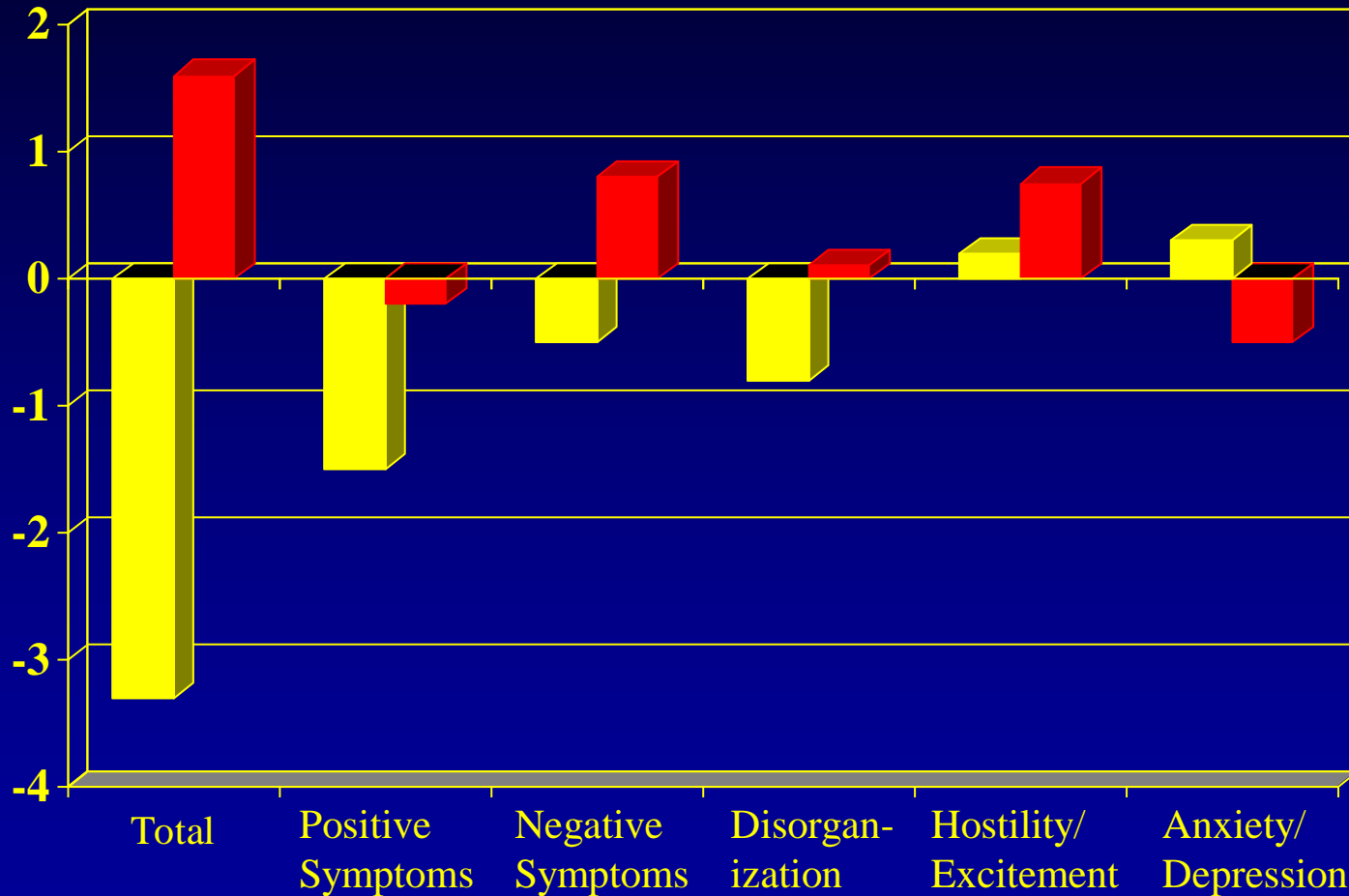
.004

.015

.076

.005

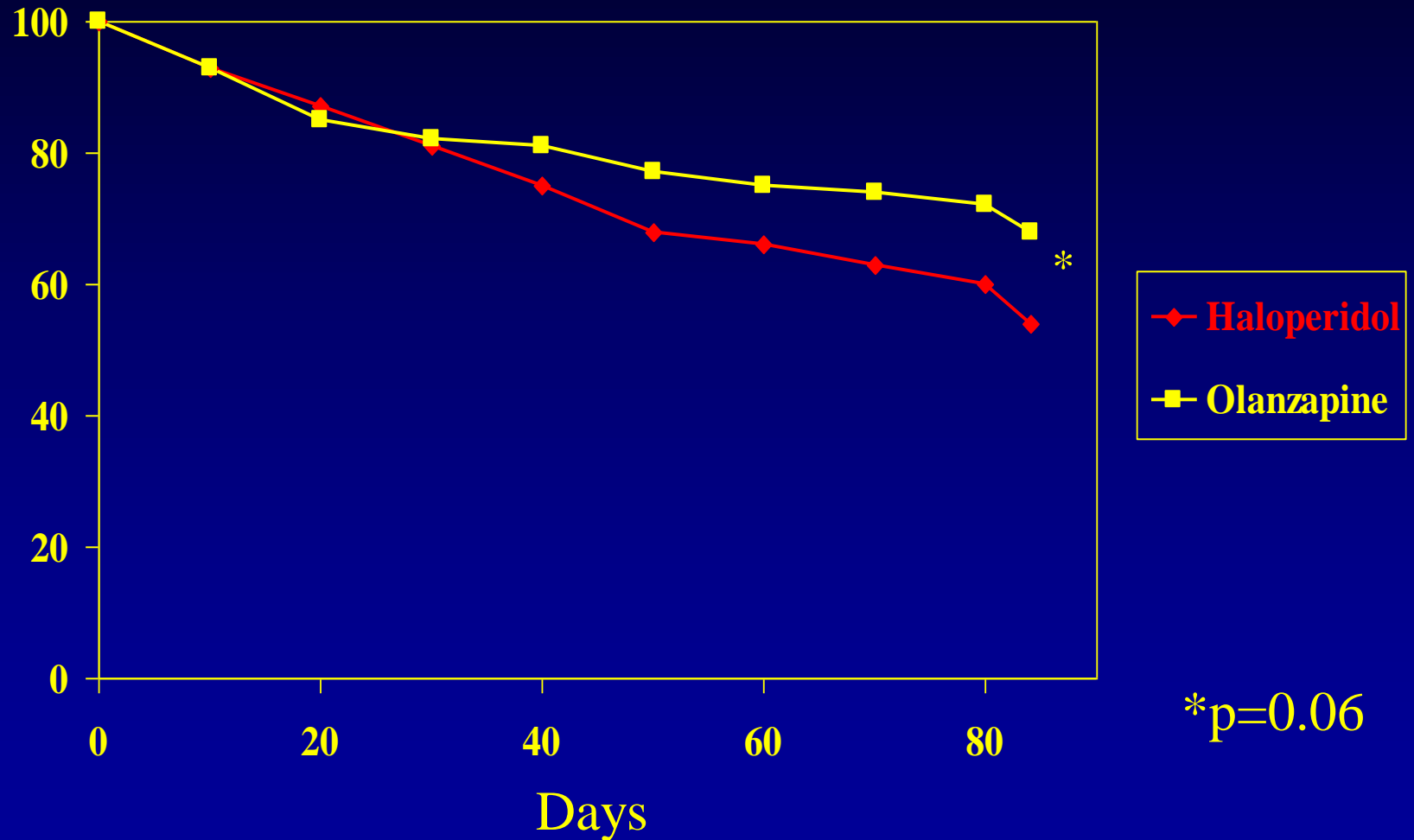
Mean
Change
in PANSS
Score



■ Risperidone
■ Haloperidol

Olanzapine for Prevention of Relapse

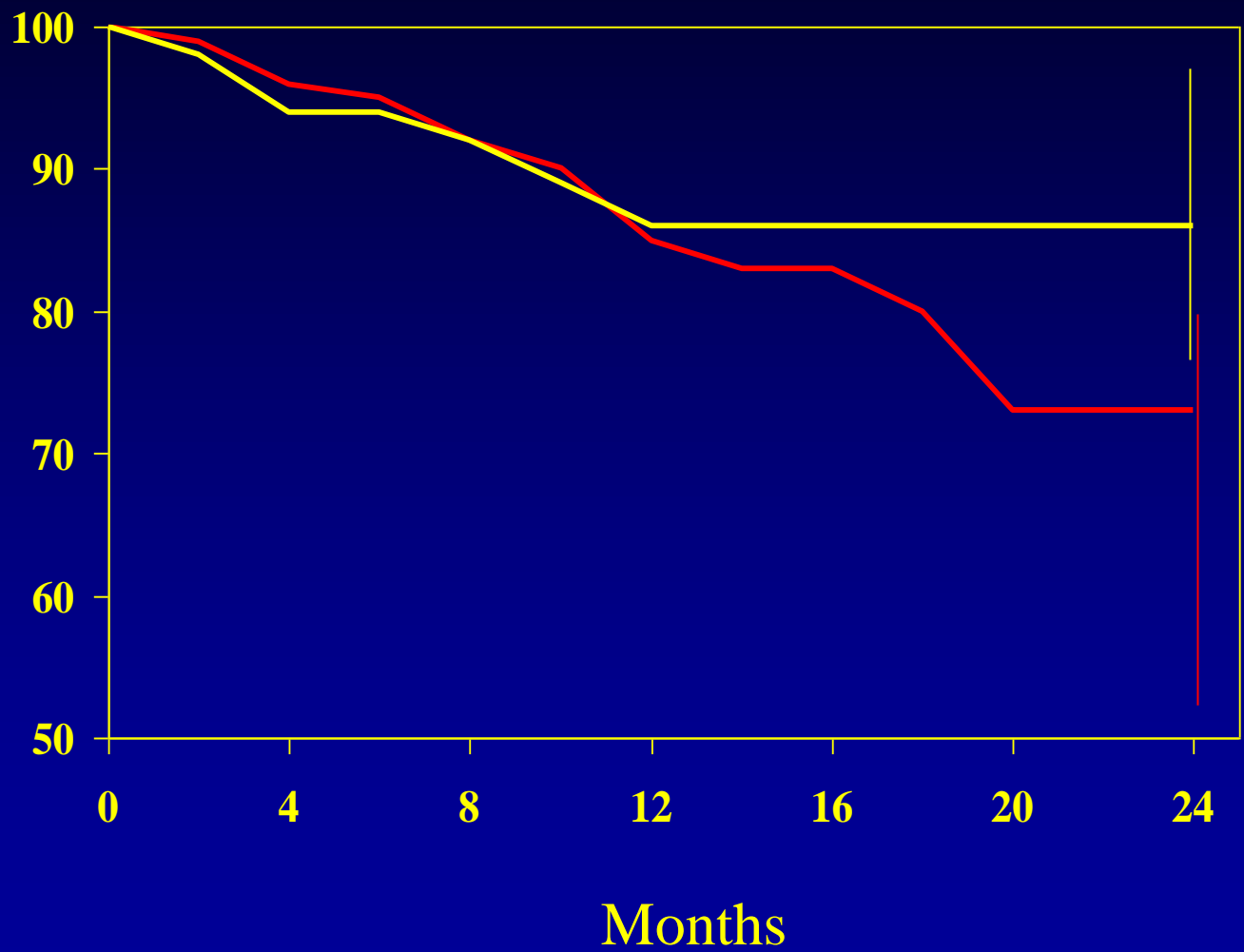
% of Patients Remaining in Study



*

Clozapine for Long-term Treatment

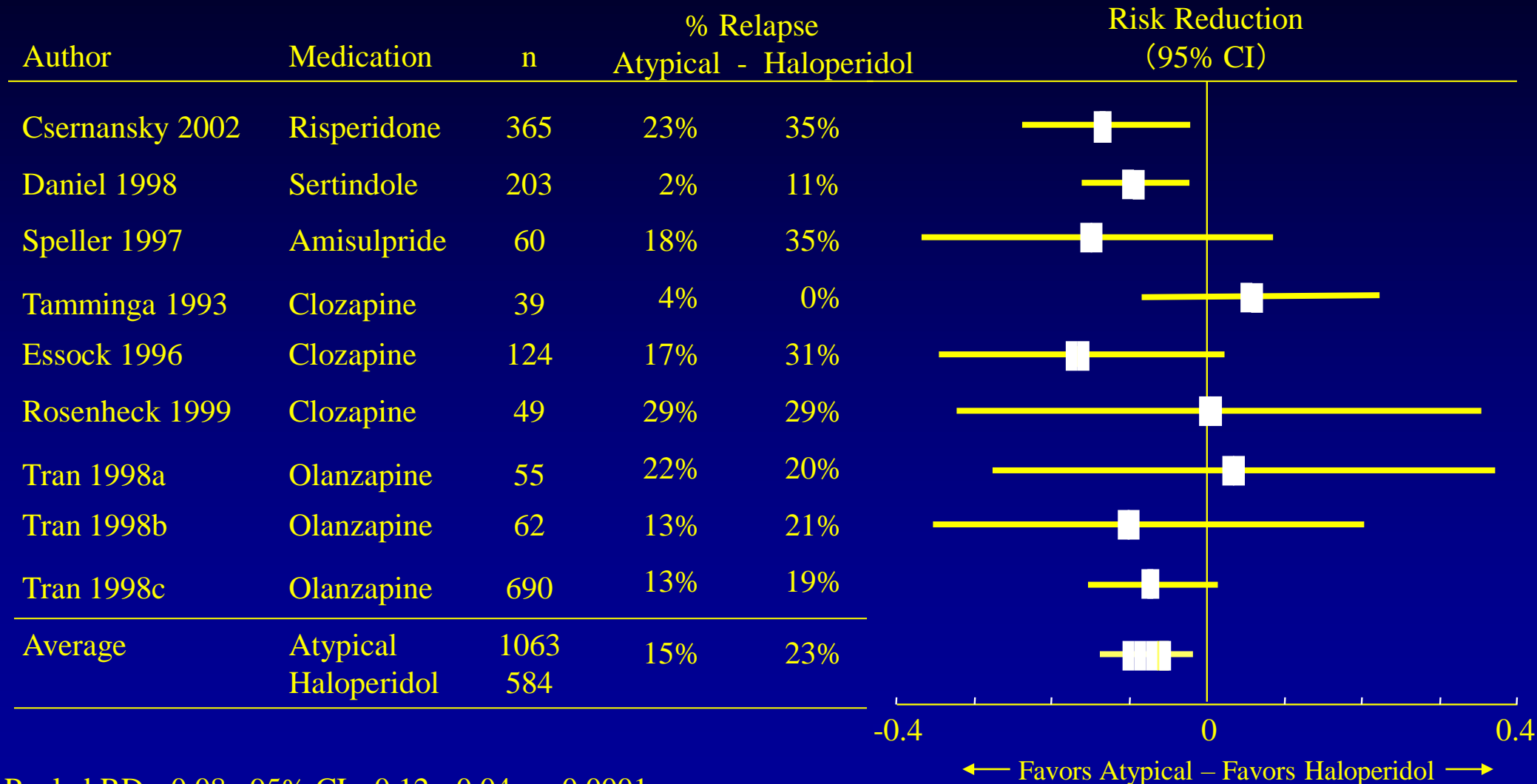
Percent of Patients Remaining Discharged



— Risperidone
— Clozapine

95% CI:
Clozapine 77-97
Risperidone 52-80

Meta-Analyses – Relapse Risk



Pooled RD: -0.08, 95% CI: -0.12, -0.04; p=0.0001

Neurocognitive Deficits



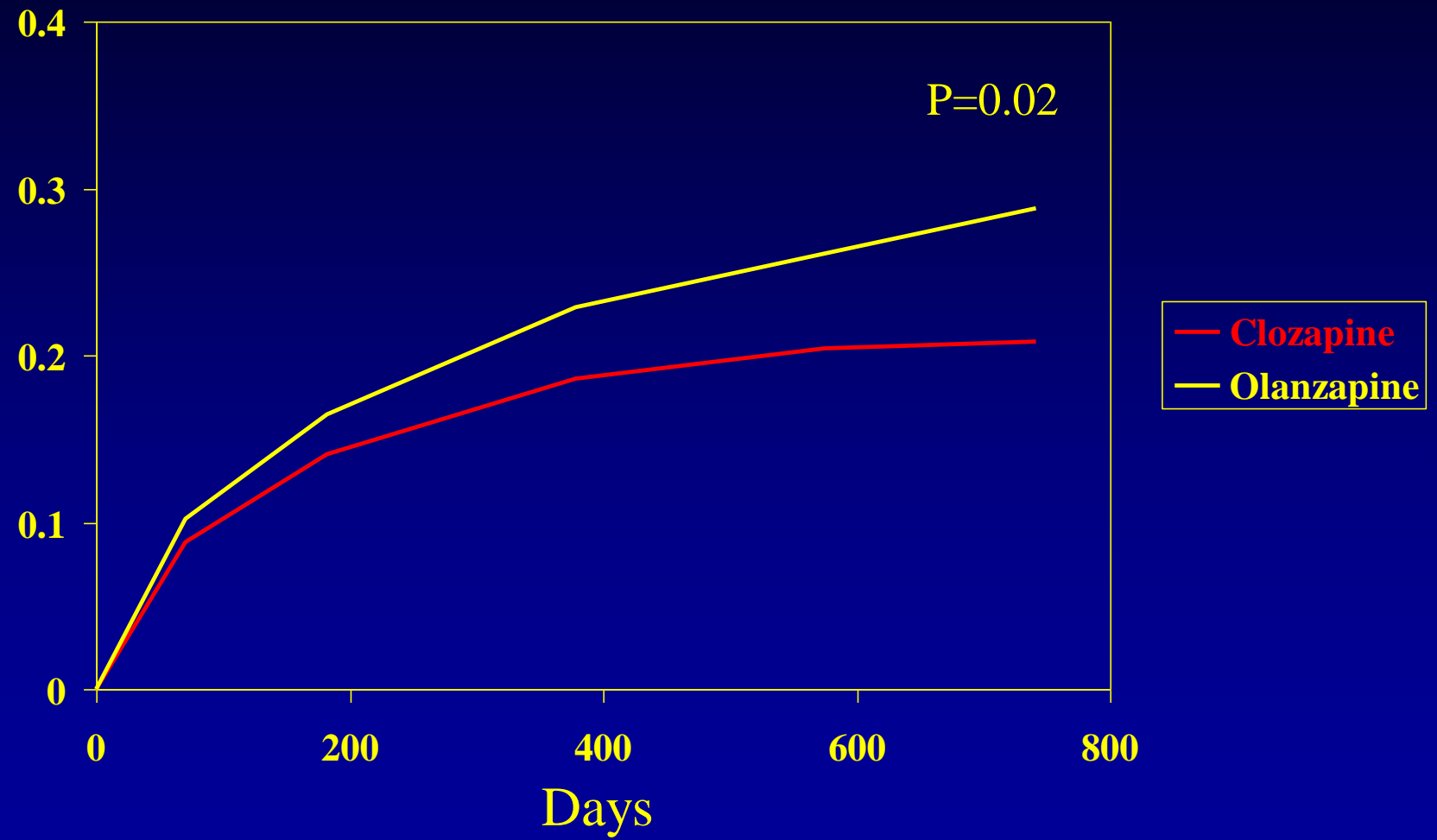
-
- Atypical antipsychotics have better cognitive profiles than conventional agents
 - Atypical antipsychotics do not return cognitive functions to normal
 - Neurocognitive benefits of atypical antipsychotics are of minor clinical significance



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Prevention of Suicide

Probability of Suicidal Ideation or Attempt



Prodromal Treatment

- Olanzapine¹ and risperidone² have been studied for prodromal treatment
- Relative risk of psychosis was 2.5-3.5 without treatment
- Benefits were less dramatic with longer treatment
- Benefits of treatment were lost within 1 year of discontinuation
- Medication may delay, rather than prevent, psychosis

1. McGlashan TH, Am J Psychiatry 2006; 163:790

2. McGorry PD, Arch Gen psychiatry 2002; 59:921



Psychosocial Interventions



WHO International Pilot Study on Schizophrenia and Determinants of Outcome

- Outcomes for schizophrenia are better in developing than industrialized countries
- Possible factors in developing countries:
 - Intact families
 - Greater community support network
 - Fewer social and occupational demands
 - Greater acceptance of psychotic behavior



Psychosocial Treatments

Strength of Evidence
For Efficacy



- Case management
- Assertive community treatment (ACT)
- Family interventions
- Social skills training
- Vocational rehabilitation
- Supportive psychotherapy



Psychotherapy

What Works

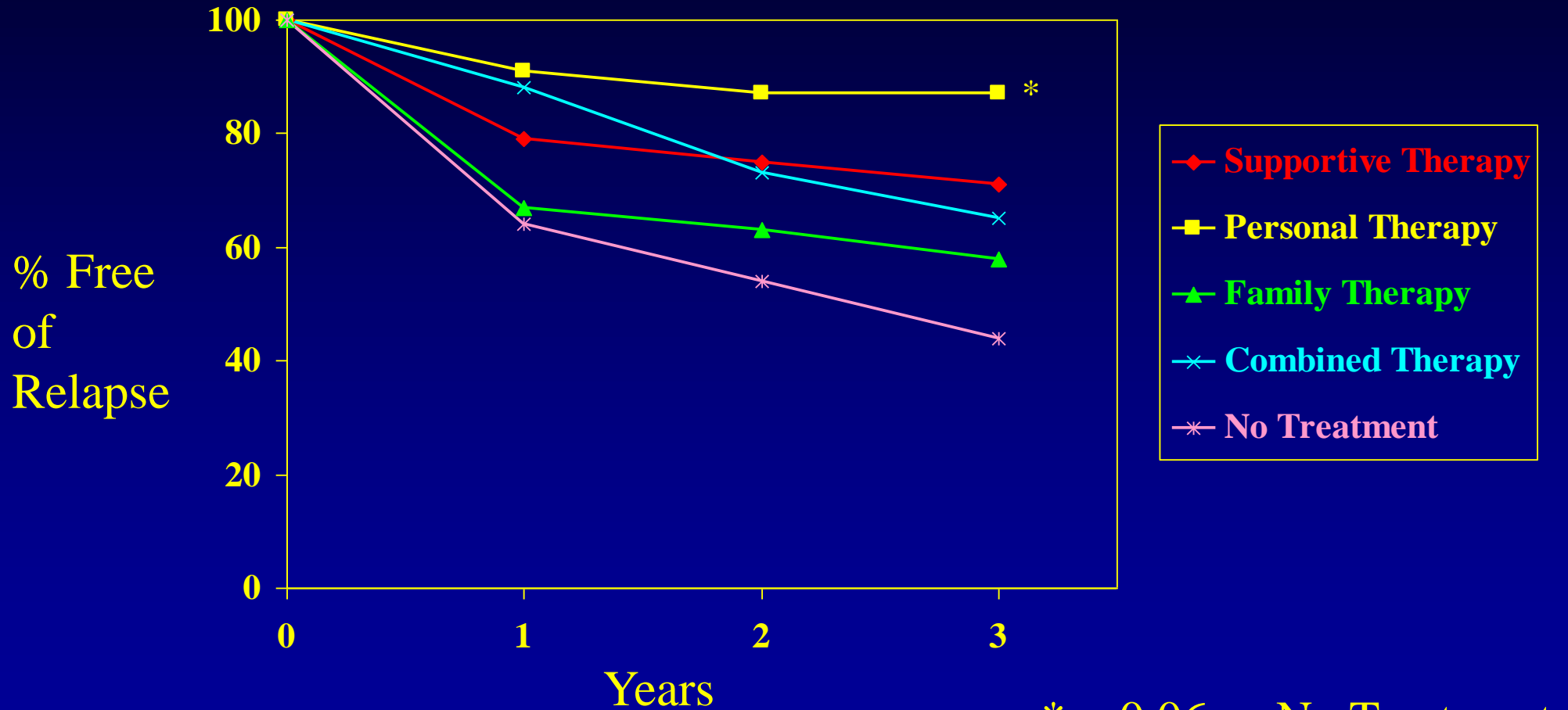
- Supportive groups
- Individual supportive Tx

What Doesn't

- Insight oriented Tx
- CBT*
- Milieu Tx

*CBT is recommended in APA Practice Guidelines (2004), but a recent review found no evidence of efficacy (Jones C, et al. Cochrane Database of Systematic Reviews 1, 2009).

Psychosocial Treatment



*p=0.06 vs No Treatment



Side Effects





Side Effects - Overview

By Class

	EPS	Orthostatic Hypotension	Anticholinergic Symptoms	Prolactin Elevation
High-potency Conventional	+++	+	+/-	++
Low-potency Conventional	++	+++	+++	++
Atypical (1 st line)	+/- to +	+/- to ++	+/- to ++	+/- to ++
Clozapine	0	+++	+++	+/-



Side Effects - Overview

By Class

	qTc Prolongation	Sedation	Weight Gain
High-potency Conventional	+/-	+	+
Low-potency Conventional	++	+++	+++
Atypical (1 st line)	+/- to +	+/- to +++	+/- to +++
Clozapine	+/- to +	+++	+++



Side Effects - Overview

Atypical Medications

	EPS	Orthostatic Hypotension	Anticholinergic Symptoms	Prolactin Elevation
Aripiprazole	+/-	+/-	+/-	+/-
Asenapine	+	+/-	+/-	+/-
Iloperidone	+/-	+/-	+	+
Olanzapine	+/-	+/-	+	+/-
Paliperidone	+	+	+/-	++
Quetiapine	+/-	++	++	+/-
Risperidone	+	+	+/-	++
Ziprasidone	+/-	+/-	+/-	+/-



Side Effects - Overview

Atypical Medications


	qTc Prolongation	Sedation	Weight Gain
Aripiprazole	+/-	+/-	+/-
Asenapine	+/-	+	+
Iloperidone	+	+	++
Olanzapine	+/-	++	+++
Paliperidone	+/-	+	++
Quetiapine	+/-	+++	++
Risperidone	+/-	+	++
Ziprasidone	+	+/-	+/-

* Extrapyramidal Symptoms (EPS)

- Akathisia (subjective sense of restlessness)
 - Stiff, rigid muscles
 - Bradykinesia (slow movements)
 - Dystonia (muscle spasms)
 - Tremor
 - Cognitive dysfunction
-

Extrapyramidal Symptoms (EPS)

Risk by class of medication

- 
- High-potency conventional neuroleptic (20-40%)
 - Low-potency conventional neuroleptic
 - Paliperidone/Risperidone
 - Aripiprazole/Olanzapine/Ziprasidone
 - Quetiapine/Clozapine

* Extrapyramidal Symptoms (EPS)

■■■ Treatment Options

- Reduce medication dose
- Slow down the rate of titration
- Consider alternative medication
- Adjunctive medication

* Extrapyramidal Symptoms (EPS)

■■■ Treatment – Adjunctive Medication

- Anticholinergic
 - Benztropine 1-2 mg bid-qid
 - Trihexyphenidyl 2-5 mg bid-qid
- Antihistamine
 - Diphenhydramine 25-50 mg bid-qid
- Dopaminergic
 - Amantadine 100 mg bid-tid



Metabolic Syndrome



-
- Prevalence of obesity and diabetes in patients with schizophrenia is 1.5-2.0 times higher than the general population
 - No studies on obesity and diabetes in drug-naïve schizophrenia patients are available



Metabolic Syndrome

■ ■ ■

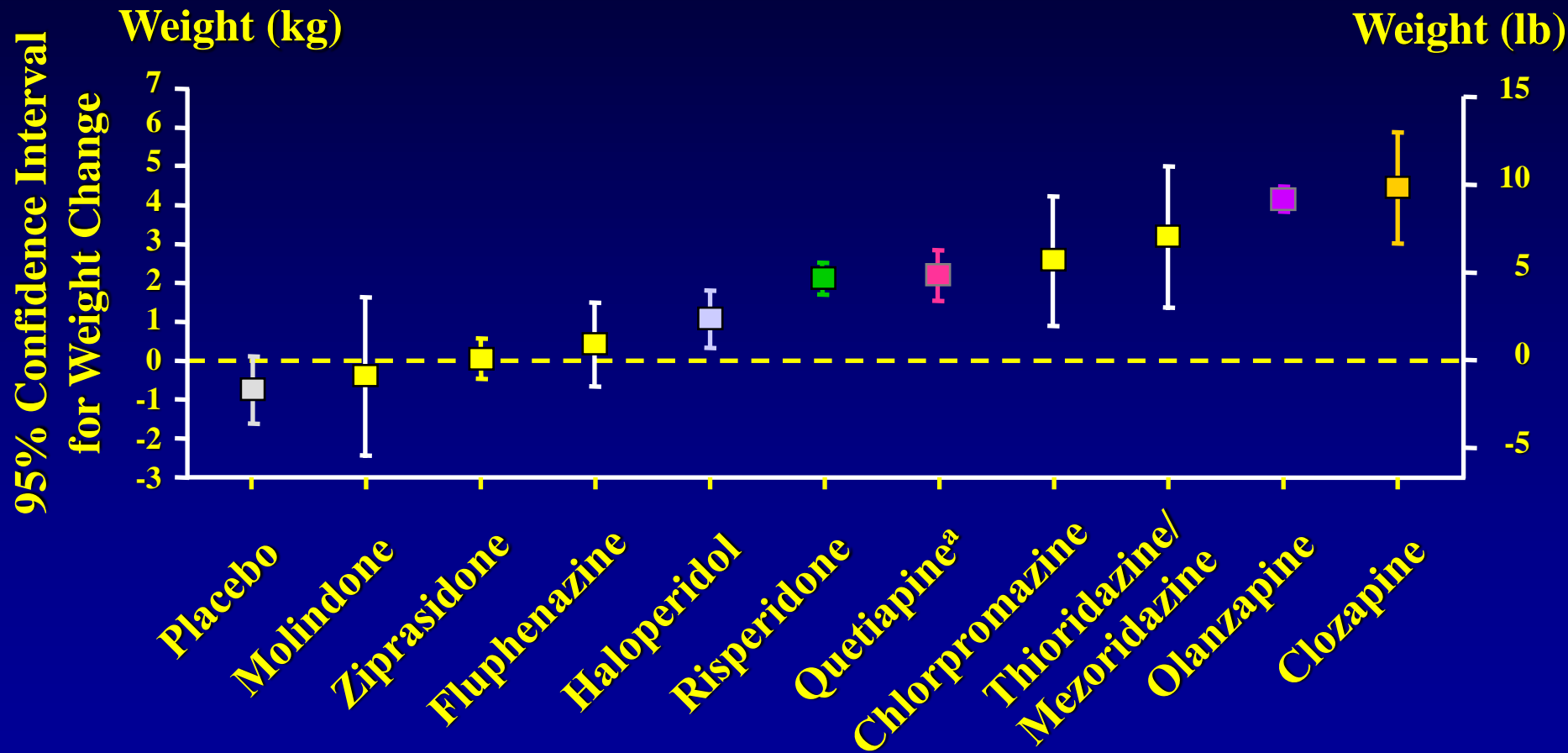
Use of atypical antipsychotics is associated with metabolic dysregulation

- Weight gain
- Type 2 diabetes
- Elevated LDL cholesterol
- Elevated triglycerides
- Decreased HDL cholesterol
- Diabetic ketoacidosis

*

Meta-analysis of Antipsychotic-related Weight Gain


Estimate at 10 Weeks^a



^a Quetiapine weight gain estimated at 6 weeks

Risk of Metabolic Complications

Relative risk of medications

- 
- Clozapine/Olanzapine/Low Potency Neuroleptics
 - Iloperidone/Paliperidone/Quetiapine/Risperidone/High Potency Neuroleptics
 - Asenapine
 - Aripiprazole/Ziprasidone

*

Metabolic Syndrome

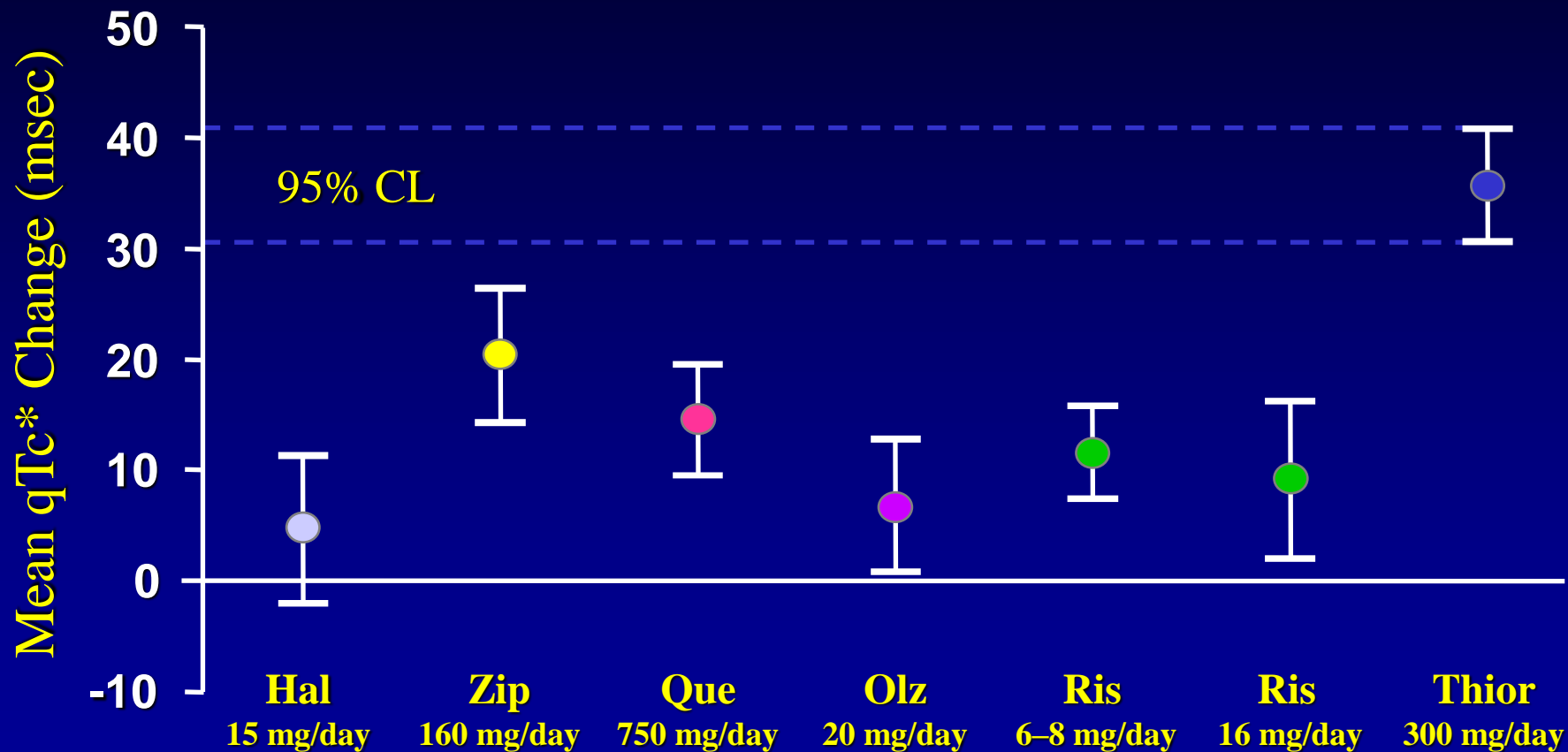
Recommended monitoring for patients on atypical antipsychotics

	Baseline	4 wks	8 wks	12 wks	Quarterly	Annual	5 yrs
Personal/family history	X					X	
Weight (BMI)	X	X	X	X	X		
Waist Circumference	X					X	
Blood pressure	X			X		X	
Fasting plasma glucose	X			X		X	
Fasting lipid profile	X			X			X

Cardiovascular Adverse Events

- Conventional low potency drugs thioridazine (Mellaril) and mesoridazine (Stelazine) are associated with qTc prolongation and increased risk of cardiac death
- Ziprasidone carries a “bold” warning regarding qTc prolongation and associated cardiac risk, but no increased incidence of cardiac mortality or morbidity has been detected with ziprasidone

Mean qTc Change at Steady-state C_{max}



*Bazett correction

Metabolic inhibition did not prolong the QTc interval with any drug studied

Data on file, Pfizer Inc. (Study 054)

Increased Mortality

- All atypical antipsychotics carry a “black box” warning of increased mortality in elderly patients with dementia-related psychosis
- Risk is comparable among all conventional and atypical antipsychotics

Increased Mortality

Meta-analysis of 15 studies of risk of typical and atypical antipsychotics in elderly patients

	Mortality	Odds Ratio
Controls	2.3%	
Atypical Antipsychotics	3.5%	1.54
Haloperidol	3.9%	1.68

Increased Mortality

Retrospective study of mortality in 22,890 elderly patients receiving antipsychotics


- Higher risk with conventional antipsychotics
OR = 1.37
- Higher risk with recent initiation of medicine
- Higher risk with higher doses

Tardive Dyskinesia

- Adverse reaction to antipsychotic medications
- Irregular, choreoathetotic movements
 - Chorea - irregular, spasmodic movements
 - Athetosis - slow writhing movements
- May occur in any muscle group
- Most common in facial, oral, and truncal muscles

Tardive Dyskinesia

Risk by class of medication:

- 
- High potency conventional neuroleptic (7%/yr)
 - Low potency conventional neuroleptic (5%/yr)
 - Atypical antipsychotics (0.5%/yr)
 - Clozapine (none reported)

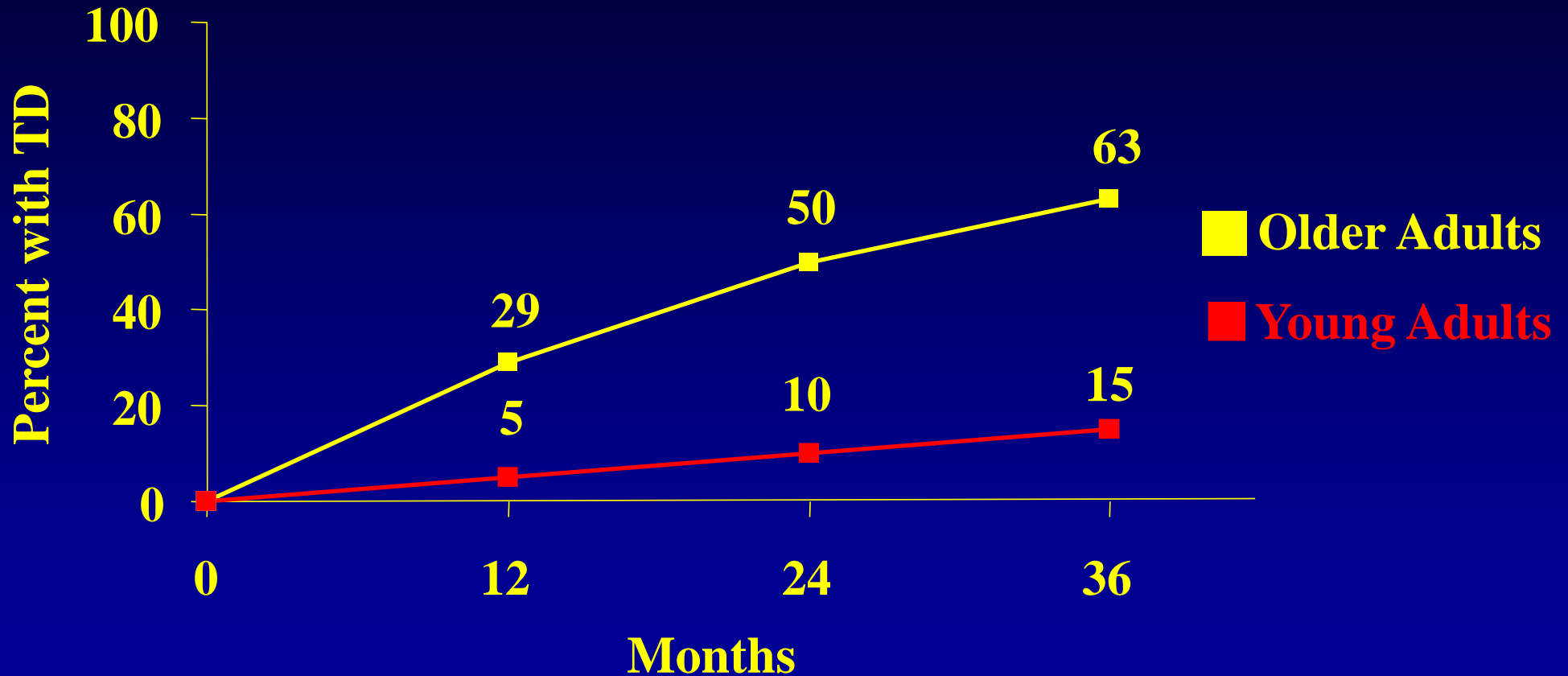
Tardive Dyskinesia

Cumulative Annual Risk of Tardive Dyskinesia

	Age 20	Age 70
Conventional Neuroleptic	5%	30%
Atypical Antipsychotic	0.5%	2.5-5%

Kane JM, et al., J Clin Psychopharmacol 1988;8:52S. Chakos MH, et al., Arch Gen Psychiatry 1996;53:313. Woerner MG, et al., Am J Psychiatry 1998;155:1521. Correll CU, et al., Am J Psychiatry 2004; 161:414. Glazer WM, J Clin Psychiatry 2000; 61 suppl 4:21.

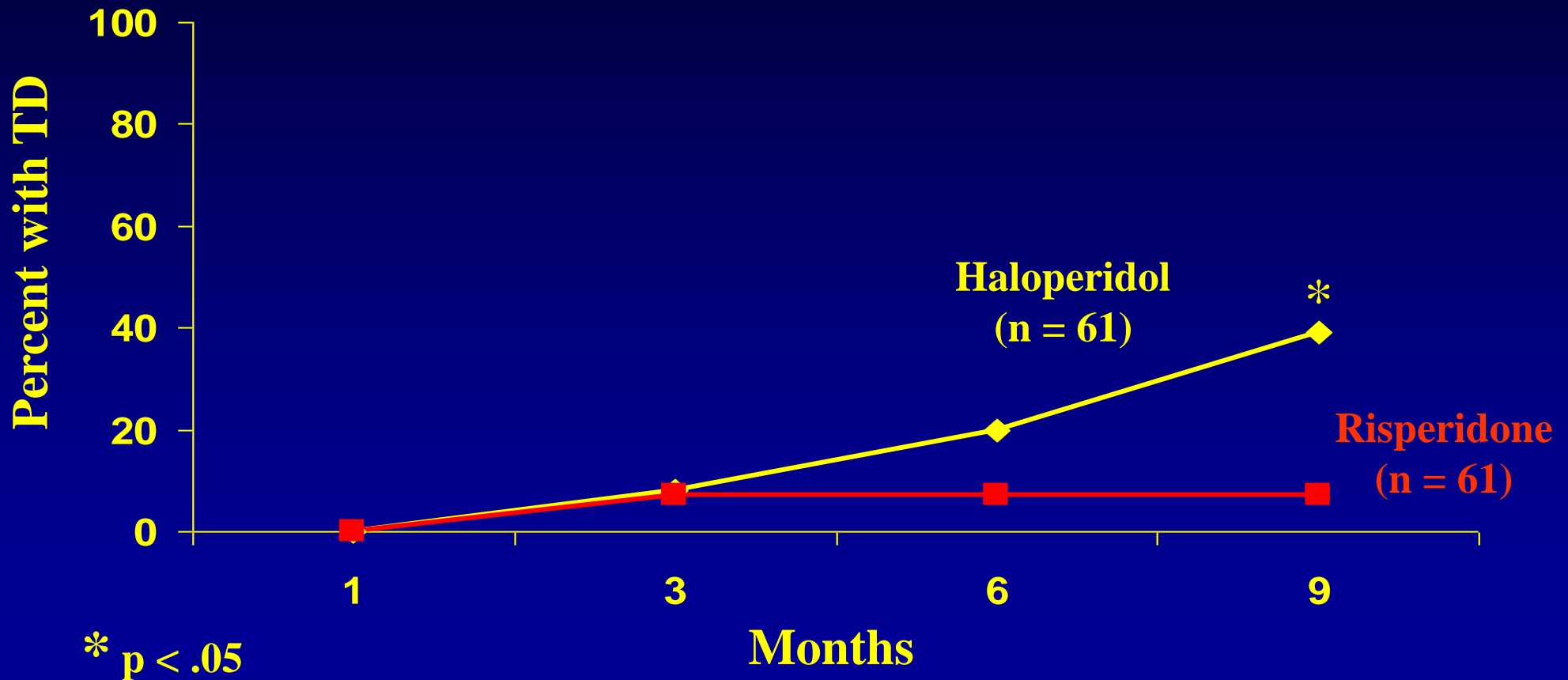
Cumulative Incidence of TD with Conventional Antipsychotics



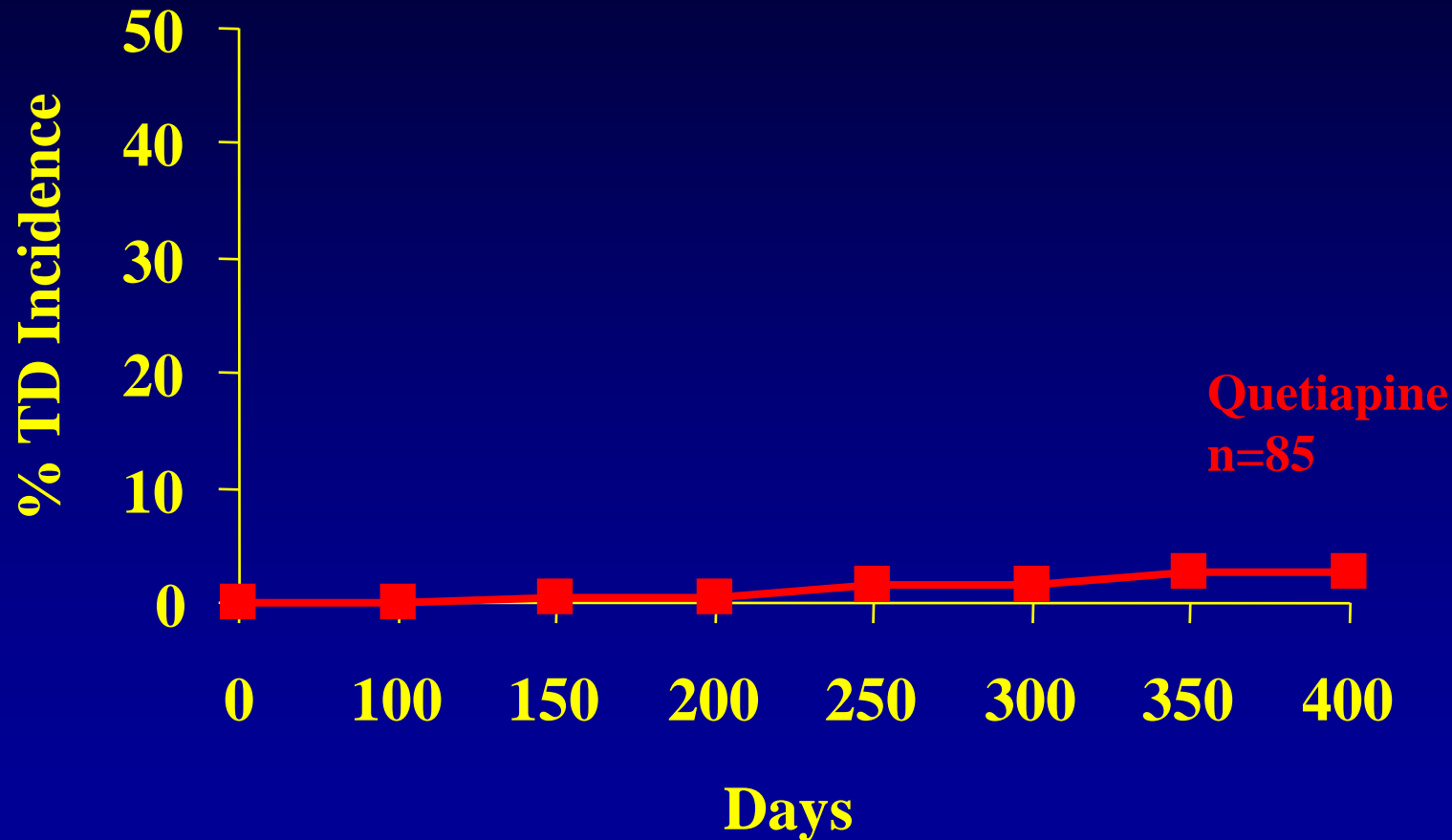
Kane JM, et al., J Clin Psychopharmacol 1988;8(4 Suppl):52S

Jeste D, et al., Am J Geriatric Psychiatry, 1999;7:70

TD Incidence in Older Patients: Haloperidol versus Risperidone (1mg/d)



Cumulative Incidence of Persistent TD With Quetiapine in Elderly Psychosis Patients



Tardive Dyskinesia

Natural History

- May spontaneously improve, remain static, or worsen
 - Static symptoms are most common
 - Spontaneous improvement is least common
- About half of patients experience relief of symptoms within 3 months of antipsychotic discontinuation

Tardive Dyskinesia



Acute Treatment


- Increase antipsychotic dose temporarily suppresses symptoms
- Benzodiazepine may bring about a modest reduction in symptoms




Tardive Dyskinesia

■ ■ ■ Maintenance Treatment

- Reduce antipsychotic dose and time of exposure
- Clozapine (standard dose)
 - 50% of patients show 50% reduction in movements
- Other treatments have not consistently been effective
 - Vitamin E
 - Benzodiazepine
 - Dopaminergic agents
 - Branched-chain amino acids



Antipsychotic Selection and Treatment Strategies



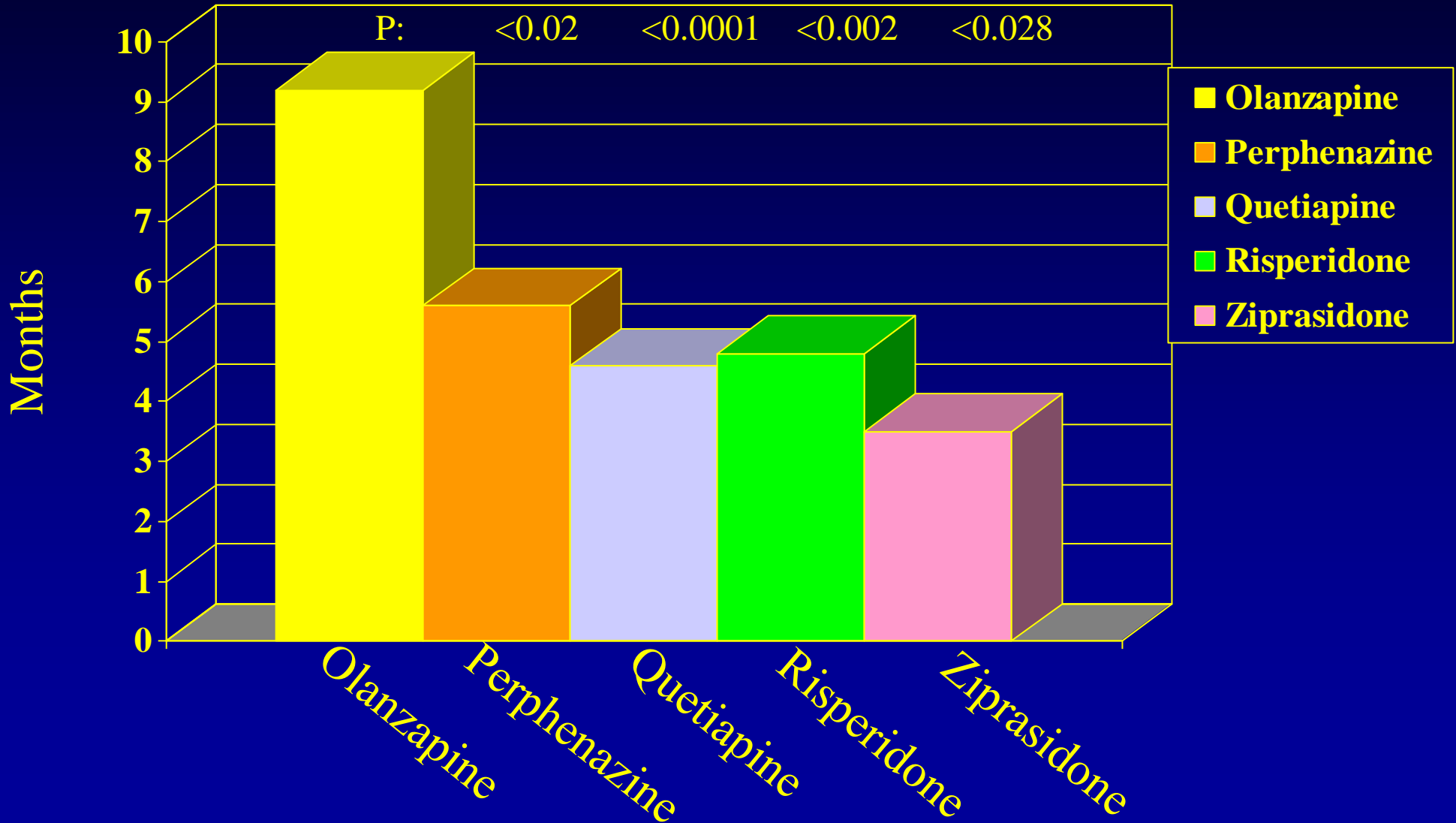
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Clinical Antipsychotic Trials of Intervention Effectiveness

- 1493 outpatients with chronic schizophrenia
 - Randomized, double-blind design
 - NIMH sponsored
 - 18 months
 - Primary outcome was duration of treatment
-

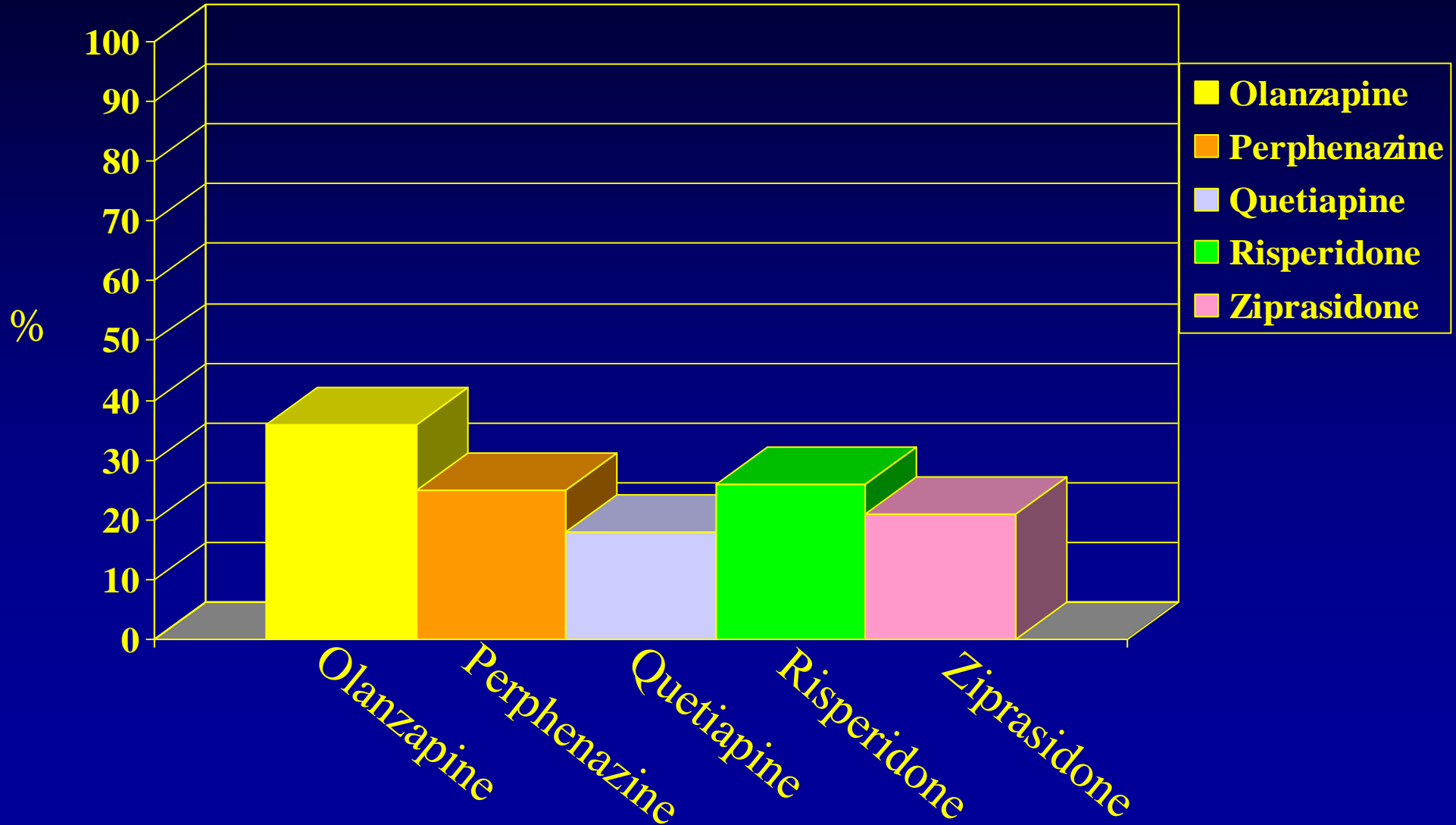
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Duration of Treatment



CATIE

Patients Completing 18 Months of Treatment



CATIE

■ ■ ■ --- Critiques

- Power was not great enough to confirm equivalent efficacy among drugs
 - Perphenazine patients were not randomly selected
 - Correction for prior treatment reduced olanzapine advantage (lost statistical significance)
 - Olanzapine dose was higher than other drugs
-

CATIE

Conclusions

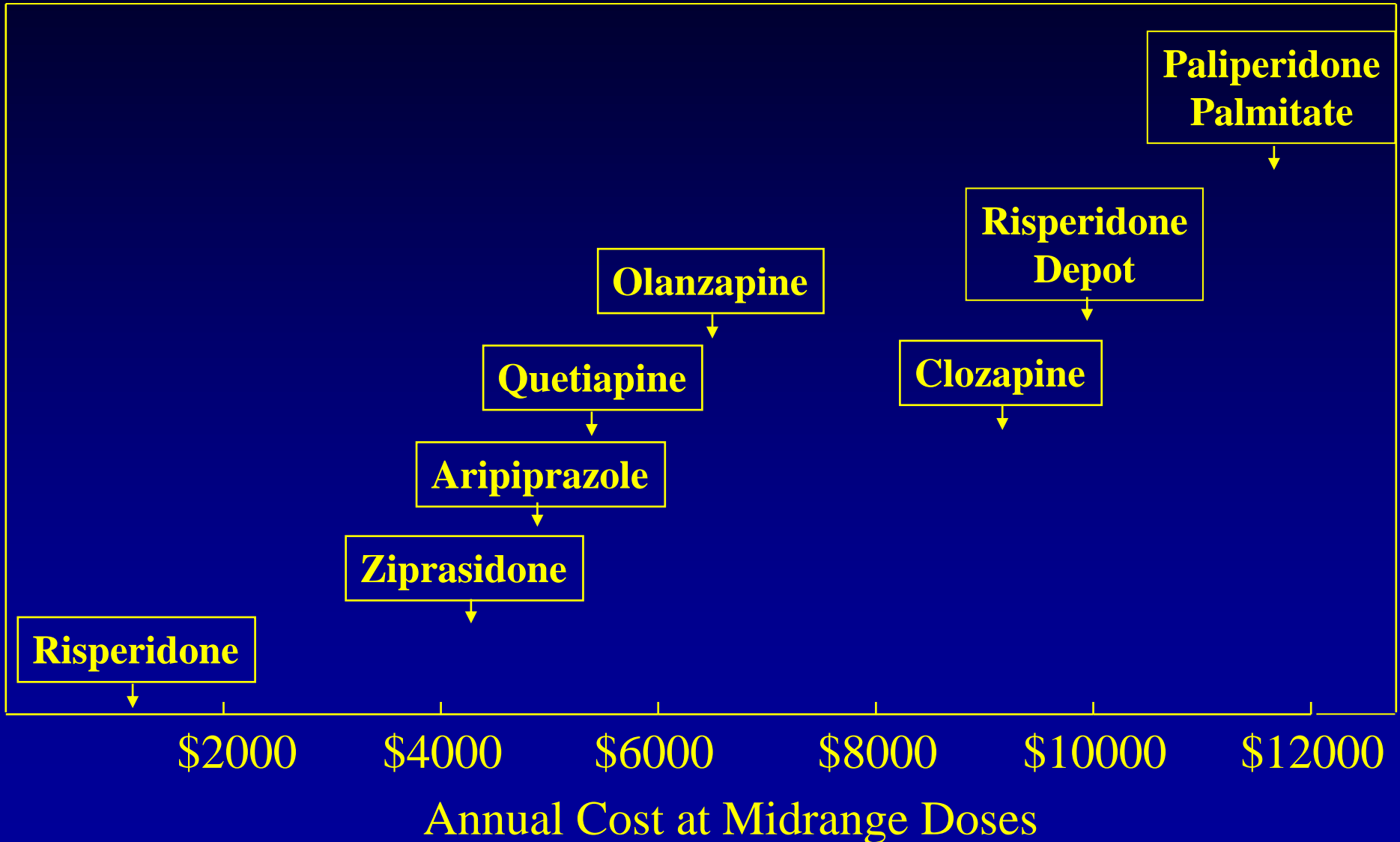
- Most patients discontinued treatment prior to 18 months, but duration of treatment differed among agents
- Tolerability of treatment was comparable among drugs, but specific side effects differed

CATIE

Conclusions

- Patients may continue treatment with olanzapine longer than with other agents
- Olanzapine was associated with greater weight gain and metabolic problems
- Perphenazine was similar to quetiapine, risperidone, and ziprasidone in efficacy but had more EPS

Relative Costs of Atypical Antipsychotic Medications



Treatment Selection with Antipsychotics

- All antipsychotics are effective against psychotic symptoms
 - Atypical antipsychotics have lower risk of EPS and TD than conventional drugs
 - Each medication has unique side effects
 - Each medication has unique pharmacokinetics
 - Individual patients may respond preferentially to different medications
-

Antipsychotic Augmentation Strategies

- Augmentation strategies have generally shown modest results
- No one strategy is generally accepted
 - Mood stabilizers
 - Benzodiazepines
 - Antidepressants
 - Antipsychotic combinations
 - ECT

Antipsychotic Combinations

- 20-25% of patients receive more than one antipsychotic
- Few data are available on efficacy and safety of antipsychotic combinations
- Anecdotal accounts of specific combinations have not been supported by formal studies
- Pharmacologic justification is weak
- Side effects tend to be additive
- Costs are always additive

Treatment Recommendations

- Continuous, full-dose antipsychotic treatment is the key to good outcome in schizophrenia
- “Lowest effective dose” strategies are associated with higher relapse rates and poorer outcomes
- Antipsychotic polypharmacy is rarely justified
- Frequent medication changes are associated with poorer outcomes

Treatment Recommendations



-
- Depot antipsychotics ensure treatment adherence
 - Clozapine should be considered for patients not responding to trials of at least 2-3 antipsychotics
 - Psychosocial treatment is essential to good outcome



Post-test



-
1. Negative symptoms of schizophrenia include:
 - a. Auditory hallucinations
 - b. Blunted affect
 - c. Depressed mood
 - d. Persecutory delusions
 - e. Thought disorganization



Post-test

-
2. Clinical efficacy of antipsychotic medications is highly correlated with:
- a. Dopamine D1 binding
 - b. Dopamine D2 binding
 - c. Serotonin binding
 - d. The ratio of D1/D2 binding
 - e. The ratio of D2/serotonin binding
-

Post-test



-
3. Clozapine is unique among antipsychotics in that it:
 - a. Has greater efficacy
 - b. Has fewer side effects
 - c. Is a dopamine D2 partial agonist
 - d. Is FDA approved for treatment of bipolar mania
 - e. Has a more favorable safety profile



Post-test

-
4. Which first-line atypical antipsychotic has the lowest risk of extrapyramidal side effects?
- a. Aripiprazole
 - b. Olanzapine
 - c. Quetiapine
 - d. Risperidone
 - e. Ziprasidone
-

Post-test



-
5. Which of the following atypical antipsychotics has the lowest risk of metabolic complications?
- a. Clozapine
 - b. Olanzapine
 - c. Quetiapine
 - d. Risperidone
 - e. Ziprasidone



Answer Key



1. b

2. b

3. a

4. c

5. e

